



A 23-year-old woman comes to the emergency department due to right wrist pain after a fall. The patient fell onto her outstretched hand while walking across the floor at a gym where she exercises regularly. She has no significant medical history and takes no medications. The patient says she has tried several diets to lose weight and is currently consuming a vegan diet. Her last menstrual period was 3 months ago. She does not use tobacco, alcohol, or illicit drugs. Temperature is 36.1 C (97 F), blood pressure is 90/58 mm Hg, and pulse is 50/min. BMI is 18.3 kg/m<sup>2</sup>. Weight is 50 kg (110.2 lb) and height is 165 cm (5 ft 5 in). Physical examination shows tenderness and swelling over the distal radius. The parotid glands are enlarged and there are fine, soft hairs on her extremities. Urine pregnancy test is negative. X-rays reveal a nondisplaced fracture of the right distal radius and generalized radiolucency of the bone. Which of the following is the most likely diagnosis?

- ☐ A. Anorexia nervosa
- ☐ B. Avoidant/restrictive food intake disorder
- ☐ C. Bulimia nervosa
- ☐ D. Pellagra
- ☐ E. Pseudo







lose weight and is currently consuming a vegan diet. Her last menstrual period was 5 months ago. She does not use tobacco, alcohol, or illicit drugs. Temperature is 36.1 C (97 F), blood pressure is 90/58 mm Hg, and pulse is 50/min. BMI is 18.3 kg/m<sup>2</sup>. Weight is 50 kg (110.2 lb) and height is 165 cm (5 ft 5 in). Physical examination shows tenderness and swelling over the distal radius. The parotid glands are enlarged and there are fine, soft hairs on her extremities. Urine pregnancy test is negative. X-rays reveal a nondisplaced fracture of the right distal radius and generalized radiolucency of the bone. Which of the following is the most likely diagnosis?

- ☐ A. Anorexia nervosa
- ☐ B. Avoidant/restrictive food intake disorder
- ☐ C. Bulimia nervosa
- ☐ D. Pellagra
- ☐ E. Rickets
- ☐ F. Scurvy

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does not use tobacco, alcohol, or illicit drugs. Temperature is 36.1 C (97 F), blood pressure is 90/58 mm Hg, and pulse is 50/min. BMI is 18.3 kg/m<sup>2</sup>. Weight is 50 kg (110.2 lb) and height is 165 cm (5 ft 5 in).

Physical examination shows tenderness and swelling over the distal radius. The parotid glands are enlarged and there are fine, soft hairs on her extremities. Urine pregnancy test is negative. X-rays reveal a nondisplaced fracture of the right distal radius and generalized radiolucency of the bone. Which of the following is the most likely diagnosis?

- ☒ A. Anorexia nervosa (66%)
- ☐ B. Avoidant/restrictive food intake disorder (6%)
- ☐ C. Bulimia nervosa (23%)
- ☐ D. Pellagra (0%)
- ☐ E. Rickets (2%)
- ☐ F. Scurvy (1%)

Correct

66%



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09/28/2020

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## Anorexia nervosa

### Epidemiology

- Increased risk in whites, industrialized countries, athletes, models
- Median onset at age 18
- 10:1 female/male ratio

### DSM-5 diagnostic criteria

- Restricted energy intake with significantly **low body weight** (BMI generally  $<18.5 \text{ kg/m}^2$ )
- Intense **fear of becoming fat** or persistent avoidance of weight gain
- **Distorted body image**, excessive influence of weight on self-worth, or persistent denial of complications related to low body weight

### Medical complications

- Osteoporosis
- Amenorrhea
- Lanugo or hair loss
- Parotid hypertrophy (if binge/purge behavior)
- Hypotension, hypothermia, bradycardia
- Cardiac atrophy, arrhythmias







This patient has a fragility fracture (ie, fracture due to low-energy trauma) and radiolucency of bone on x-ray, suggesting **osteoporosis**. In light of her restricted diet, thin body habitus, and cessation of menses, this is likely due to a low-estrogen state and **functional hypothalamic amenorrhea** (excessive exercise or weight loss suppresses secretion of GnRH, leading to decreased release of FSH and low estrogen levels). She also has vital sign abnormalities (eg, bradycardia, low body temperature) and lanugo (ie, fine, downy body hair) that together raise suspicion for **anorexia nervosa** (AN).

AN is characterized by **restriction of energy intake** below that needed to maintain normal body weight (BMI typically  $<18.5 \text{ kg/m}^2$ ), leading to an emaciated body habitus and clinical features of starvation.

Patients with AN have a distorted body image and an intense fear of gaining weight or becoming fat.

Common behaviors include excessive caloric restriction, intensive exercise, and binge eating/purging (eg, self-induced vomiting, misuse of laxatives or diuretics).

**(Choice B)** Avoidant/restrictive food intake disorder is characterized by inadequate food intake due to lack of interest in eating, dislike of the sensory experience of eating, or concerns about the consequences of eating without an associated disturbance in body image. This disorder typically presents in childhood or adolescence, and patients do not have signs of recurrent vomiting (eg, parotid hypertrophy, as in this patient).





eating without an associated disturbance in body image. This disorder typically presents in childhood or adolescence, and patients do not have signs of recurrent vomiting (eg, parotid hypertrophy, as in this patient).

**(Choice C)** Bulimia nervosa is characterized by recurrent binge eating/purging and preoccupation with body image, much like in many patients with AN. However, patients with bulimia maintain their body weight at or above the minimally normal level and do not experience the signs of starvation that are present in this patient.

**(Choice D)** Pellagra (ie, niacin deficiency) is characterized by dementia, dermatitis, and diarrhea.

**(Choice E)** Vegan diets, which are free from animal products, can increase the risk for deficiencies of vitamin B<sub>12</sub>, calcium, and vitamin D. Vitamin D deficiency may lead to low bone density and fragility fracture. However, rickets involves deficient mineralization and disruption of the growth plates and only occurs in children.

**(Choice F)** Scurvy (ie, vitamin C deficiency) is characterized by skin and mucosal hemorrhages, intraarticular bleeding, gingival swelling, impaired wound healing, and weakened immune response to local infections. Vitamin C is readily found in plant products; a vegan diet would not predispose to scurvy.





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### Educational objective:

Anorexia nervosa is an eating disorder characterized by low body weight, intense fear of becoming fat, and distorted body image. Medical complications due to starvation in anorexia include bradycardia, hypotension, osteoporosis, and amenorrhea.

### References

- Bone health in anorexia nervosa.

Behavioral science    Gastrointestinal & Nutrition    Anorexia nervosa  
 Subject    System    Topic





A 34-year-old man comes to the emergency department due to 5 days of progressive anorexia, nausea, and abdominal pain. The patient is a known hepatitis B carrier. He admits to using IV drugs and has shared needles with other drug users on several occasions. His temperature is 37.7 C (99.9 F). Examination shows scleral icterus and mild, tender hepatomegaly. Laboratory studies are notable for highly elevated levels of liver aminotransferases and serum bilirubin and also show the following results:

Hepatitis B surface antigen	positive
Hepatitis C virus antibody	negative
HIV-1 antibody	negative
Hepatitis D RNA	positive

This patient's chronic infection assists which of the following life cycle aspects of the current infectious agent?



A. Coating of viral particles





Hepatitis C virus

antibody

negative

HIV-1 antibody

negative

Hepatitis D RNA

positive

This patient's chronic infection assists which of the following life cycle aspects of the current infectious agent?

- ☐ A. Coating of viral particles
- ☐ B. Integration into host genome
- ☐ C. Intracellular survival
- ☐ D. Replication of viral RNA
- ☐ E. Translation of viral transcripts

**Submit**



Hepatitis C virus antibody	negative
HIV-1 antibody	negative
Hepatitis D RNA	positive

This patient's chronic infection assists which of the following life cycle aspects of the current infectious agent?

- ☒ A. Coating of viral particles (39%)
- ☐ B. Integration into host genome (17%)
- ☐ C. Intracellular survival (11%)
- ☐ D. Replication of viral RNA (25%)
- ☐ E. Translation of viral transcripts (6%)





Often referred to as the delta agent, **hepatitis D virus (HDV)** is a 35-nm, double-shelled particle that resembles the Dane particle of hepatitis B virus (HBV). The internal polypeptide assembly of HDV is designated **hepatitis D antigen (HDAg)**. Associated with this antigen is a very short, circular molecule of single-stranded RNA. HDAg is considered **replication defective** as it must be coated by the external coat **hepatitis B surface antigen (HBsAg)** of HBV to penetrate the hepatocyte. HDV infection can arise either as an acute coinfection with HBV or as a superinfection of a chronic HBV carrier.

**(Choices B, C, D, and E)** Once coated with HBsAg, HDV is able to penetrate the hepatocyte, survive within the cell, integrate into the host genome, replicate its viral RNA, and translate its genome into protein.

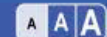
### Educational objective:

The hepatitis B surface antigen of hepatitis B virus must coat the hepatitis D antigen of hepatitis D virus before it can infect hepatocytes and multiply.

### References

- [Life cycle and pathogenesis of hepatitis D virus: A review.](#)

Microbiology
Gastrointestinal & Nutrition
Hepatitis d  
Subject
System
Topic



A 64-year-old man comes to the office due to acute-onset right upper quadrant abdominal pain, nausea, and vomiting. The patient had an extensive small bowel resection due to bowel ischemia a year ago and has been receiving total parenteral nutrition since then. His other medical problems include atrial fibrillation and hypertension. Examination shows right upper quadrant tenderness on deep palpation. Initial laboratory studies show moderate leukocytosis with normal hepatic transaminase, amylase, and lipase levels. Abdominal ultrasonography reveals gallstones and edema of the gallbladder wall. Review of prior records indicates that he had no gallstones noted on abdominal imaging performed prior to the bowel resection. Which of the following is most likely responsible for the development of gallstones in this patient?

- ☐ A. Decreased cholecystokinin release due to lack of enteral stimulation
- ☐ B. Decreased cholesterol conversion to bile acids due to liver dysfunction
- ☐ C. High cholesterol content of the nutritional fluids
- ☐ D. Inadequate supplementation of essential fatty acids
- ☐ E. Increased gastrin release in response to parenteral amino acids





and vomiting. The patient had an extensive **small bowel resection** due to bowel ischemia a year ago and has been receiving **total parenteral nutrition** since then. His other medical problems include atrial fibrillation and hypertension. Examination shows right upper quadrant tenderness on deep palpation. Initial laboratory studies show moderate leukocytosis with normal hepatic transaminase, amylase, and lipase levels. Abdominal ultrasonography reveals gallstones and edema of the gallbladder wall. Review of prior records indicates that he had no gallstones noted on abdominal imaging performed prior to the bowel resection. Which of the following is most likely responsible for the development of gallstones in this patient?

- ☒ A. Decreased cholecystokinin release due to lack of enteral stimulation (84%)
- ☐ B. Decreased cholesterol conversion to bile acids due to liver dysfunction (3%)
- ☐ C. High cholesterol content of the nutritional fluids (7%)
- ☐ D. Inadequate supplementation of essential fatty acids (3%)
- ☐ E. Increased gastrin release in response to parenteral amino acids (0%)

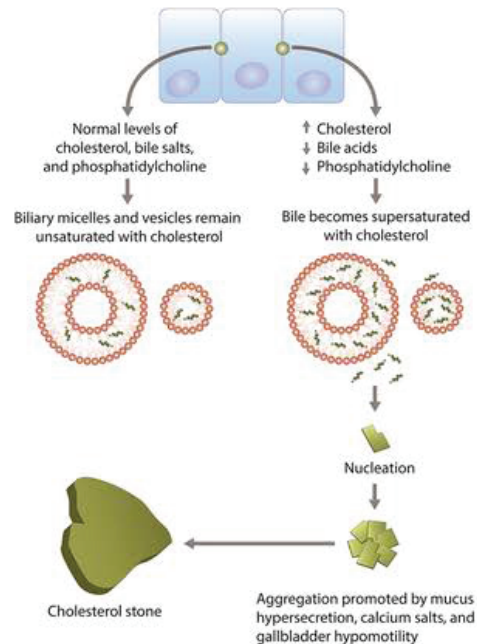




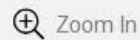


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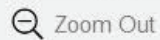
## Pathogenesis of cholesterol gallstones



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Cholesterol is secreted in bile, where it is solubilized by bile salts and phosphatidylcholine. If there is more cholesterol than can be dissolved by the bile salts, the cholesterol will precipitate into insoluble crystals, leading to the formation of **gallstones**. Risk factors for gallstone formation include obesity or rapid weight loss, female sex, glucose intolerance, and hypomotility of the gallbladder (eg, pregnancy, prolonged fasting).

A prolonged course of **total parenteral nutrition** (TPN) is often complicated by gallstones. In normal individuals, enteral passage of fat and amino acids into the duodenum triggers release of cholecystokinin (CCK), leading to contraction of the gallbladder. The absence of normal enteral stimulation in patients receiving TPN leads to **decreased CCK release** and subsequent **biliary stasis**. In addition, patients with extensive resection of the ileum can have disruption to the normal enterohepatic circulation of bile acids, leading to inadequate solubilization of biliary cholesterol and formation of cholesterol crystals.

**(Choice B)** Advanced liver disease can impair cholesterol conversion to bile acids due to the diminished synthetic ability of injured hepatocytes, leading to supersaturation of the bile with cholesterol. This contributes to the increased risk of gallstones seen in cirrhotic individuals but would be unlikely in this patient with no evidence of hepatocellular dysfunction.

**(Choice C)** TPN preparations contain glucose, amino acids, and fats based on the individual patient's





**(Choice C)** TPN preparations contain glucose, amino acids, and fats based on the individual patient's needs, with additional electrolytes, vitamins, minerals, and trace elements in carefully calculated amounts. Serum triglyceride levels may rise on TPN, but TPN does not contain significant amounts of cholesterol, and serum cholesterol levels do not usually change significantly.

**(Choice D)** Deficient supplementation of essential fatty acids in TPN is associated with a number of clinical complications, including dermatitis, alopecia, neuropathy, visual disturbances, and ataxia. Gallstones are not related.

**(Choice E)** Digested peptides and free amino acids in the gastric lumen are a major stimulus for gastrin release, so parenteral nutrition typically results in decreased (not increased) gastrin levels. Moreover, gastrin is not a significant factor in the formation of gallstones.

### Educational objective:

The absence of normal enteral stimulation in patients receiving total parenteral nutrition leads to decreased cholecystokinin release, biliary stasis, and increased risk of gallstones. Resection of the ileum can also increase the risk of gallstones due to disruption of normal enterohepatic circulation of bile acids.

Pathophysiology

Gastrointestinal & Nutrition

Gallstone disease







A 23-year-old man is referred to the gastroenterology clinic due to a 3-year history of recurring abdominal pain accompanied by cramps and diarrhea. The patient has noticed an increased frequency of episodes lately with worsening pain. He also says that his urine occasionally appears dark brown and his urine stream sometimes sputters. Imaging studies reveal a colovesical fistula. Biopsy obtained during colonoscopy shows chronic ileocolitis with discontinuous transmural inflammation and noncaseating granulomas. When given the diagnosis of Crohn disease, the patient becomes skeptical and says, "There's no way I'm getting a colostomy bag." He then refuses treatment and pursues a second opinion once his symptoms subside. A second biopsy demonstrates reduced inflammation in regions of previously active ileocolitis. An increase in which of the following cytokines is most likely responsible for this patient's clinical regression?

- ☐ A. IL-1
- ☒ B. IL-5
- ☐ C. IL-10
- ☐ D. IL-12
- ☐ E. Interferon gamma

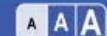




stream sometimes sputters. Imaging studies reveal a colovesical fistula. Biopsy obtained during colonoscopy shows chronic ileocolitis with discontinuous transmural inflammation and noncaseating granulomas. When given the diagnosis of Crohn disease, the patient becomes skeptical and says, "There's no way I'm getting a colostomy bag." He then refuses treatment and pursues a second opinion once his symptoms subside. A second biopsy demonstrates reduced inflammation in regions of previously active ileocolitis. An increase in which of the following cytokines is most likely responsible for this patient's clinical regression?

- ☐ A. IL-1
- ☐ B. IL-5
- ☐ C. IL-10
- ☐ D. IL-12
- ☐ E. Interferon gamma
- ☐ F. Tumor necrosis factor-alpha

**Submit**



colonoscopy shows chronic ileocolitis with discontinuous transmural inflammation and noncaseating granulomas. When given the diagnosis of Crohn disease, the patient becomes skeptical and says, "There's no way I'm getting a colostomy bag." He then refuses treatment and pursues a second opinion once his symptoms subside. A second biopsy demonstrates reduced inflammation in regions of previously active ileocolitis. An increase in which of the following cytokines is most likely responsible for this patient's clinical regression?

- ☐ A. IL-1 (0%)
- ☐ B. IL-5 (1%)
- ☒ C. IL-10 (72%)
- ☐ D. IL-12 (6%)
- ☐ E. Interferon gamma (9%)
- ☐ F. Tumor necrosis factor-alpha (8%)

Correct

72%



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09/24/2020

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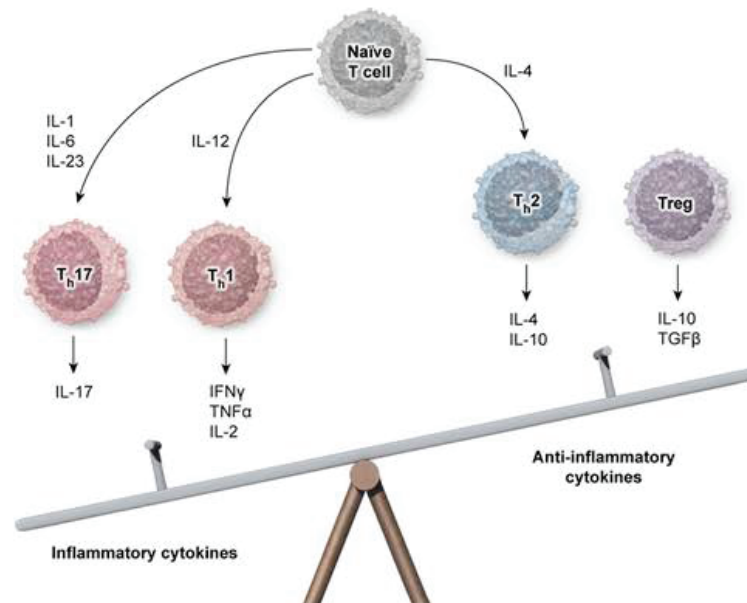
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## Exhibit Display

## Inflammatory &amp; anti-inflammatory cytokines



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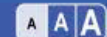
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The balance of pro- and anti-inflammatory cytokines in the intestinal mucosa is essential for homeostasis. Overproduction of proinflammatory cytokines leads to pathology such as that observed in inflammatory bowel diseases. Among the listed choices, **IL-10** is the only cytokine with **anti-inflammatory** properties. IL-10 reduces production of proinflammatory T<sub>H</sub>1 cytokines (IL-2 and interferon gamma) and major histocompatibility complex class II expression (important for antigen presentation and T-helper cell response). It also inhibits activated dendritic cells and macrophages. These effects of IL-10 result in the attenuation of cellular-mediated immunity with some enhancement of the humoral response, leading to a protective effect in Crohn disease.

**(Choice A)** IL-1, produced by macrophages and epithelial cells, has proinflammatory properties such as endothelium activation, increased chemokine expression (promoting leukocyte recruitment), and induction of fever. IL-1 $\beta$  is important for differentiation of T<sub>H</sub>17 cells.

**(Choice B)** IL-5 is secreted by T<sub>H</sub>2 cells and promotes the humoral response by stimulating differentiation of B cells and increasing IgA production. It also promotes the growth and differentiation of eosinophils and is implicated in the pathogenesis of many allergic diseases (eg, asthma).

**(Choice D)** IL-12 is secreted by macrophages and induces differentiation of T<sub>H</sub>1 cells and activation of natural killer cells.





is implicated in the pathogenesis of many allergic diseases (eg, asthma).

**(Choice D)** IL-12 is secreted by macrophages and induces differentiation of  $T_H1$  cells and activation of natural killer cells.

**(Choice E)** Interferon gamma is secreted by  $T_H1$  cells and promotes proinflammatory pathways by activating macrophages, increasing antigen presentation, and inducing the death of epithelial cells.

**(Choice F)** Tumor necrosis factor–alpha, produced by macrophages, natural killer cells, and T cells, is a proinflammatory mediator that promotes leukocyte recruitment and activates the endothelium (increases expression of adhesion molecules).

### Educational objective:

Of the cytokines released in the setting of tissue injury, IL-10 plays important anti-inflammatory and immunomodulatory roles, especially in the pathogenesis of inflammatory bowel disease. IL-10 attenuates the immune response through the inhibition of  $T_H1$  cytokines, reduction of major histocompatibility complex class II expression, and suppression of activated macrophages and dendritic cells.

### References

- [Role of cytokines in inflammatory bowel disease.](#)
- [Recent advances in cytokines: therapeutic implications for inflammatory bowel diseases](#)







A 32-year-old woman comes to the office due to 6 months of persistent diarrhea. She has had 8-10 episodes a day of tea-colored, odorless, watery stools. The symptoms have persisted despite a lactose-free diet and a fasting trial. The patient has had no abdominal pain, fever, or vomiting. Temperature is 36.7 C (98 F). Abdominal examination is unremarkable. Sampling of her gastric contents shows a total lack of gastric acid secretion. Somatostatin treatment promptly relieves the symptoms. An excess of which of the following hormones is most likely responsible for this patient's symptoms?

- ☐ A. Cholecystokinin
- ☐ B. Gastrin
- ☐ C. Ghrelin
- ☐ D. Glucagon
- ☐ E. Motilin
- ☐ F. Vasoactive intestinal peptide

**Submit**



A 32-year-old woman comes to the office due to 6 months of persistent diarrhea. She has had 8-10 episodes a day of tea-colored, odorless, watery stools. The symptoms have persisted despite a lactose-free diet and a fasting trial. The patient has had no abdominal pain, fever, or vomiting. Temperature is 36.7 C (98 F). Abdominal examination is unremarkable. Sampling of her gastric contents shows a total lack of gastric acid secretion. Somatostatin treatment promptly relieves the symptoms. An excess of which of the following hormones is most likely responsible for this patient's symptoms?

- ☐ A. Cholecystokinin (15%)
- ☐ B. Gastrin (8%)
- ☐ C. Ghrelin (2%)
- ☐ D. Glucagon (3%)
- ☐ E. Motilin (7%)
- ☒ F. Vasoactive intestinal peptide (63%)





This patient has secretory diarrhea, distinguished from inflammatory diarrhea by the absence of blood or pus and from osmotic diarrhea (eg, due to lactose intolerance) by its failure to improve with dietary modification. Excess **vasoactive intestinal peptide (VIP)** secretion due to a pancreatic islet cell tumor called VIPoma can result in **watery diarrhea, hypokalemia, and achlorhydria (WDHA) syndrome (pancreatic cholera)**. VIP stimulates pancreatic bicarbonate and chloride secretion, and its binding to intestinal epithelial cells leads to adenylate cyclase activation and increased cyclic AMP production, causing sodium, chloride, and water secretion into the bowel (**secretory watery diarrhea**, often >3 L/day).

**Somatostatin** (octreotide) decreases the production of many gastrointestinal (GI) hormones (eg, VIP, gastrin, glucagon, cholecystokinin [CCK]). Its inhibition of VIP production by this VIPoma is responsible for the resolution of this patient's symptoms.

**(Choice A)** CCK causes increased secretion of pancreatic enzymes and bicarbonate, gallbladder contraction, and inhibition of gastric emptying. It does not cause WDHA syndrome. CCK is produced by I cells of the proximal small bowel mucosa in response to fatty acids and amino acids.

**(Choice B)** Gastrin is produced by G cells in the stomach mucosa. It stimulates gastric acid production and growth of the gastric mucosa. Gastrinomas classically cause intractable peptic ulcer disease







cells of the proximal small bowel mucosa in response to fatty acids and amino acids.

**(Choice B)** Gastrin is produced by G cells in the stomach mucosa. It stimulates gastric acid production and growth of the gastric mucosa. Gastrinomas classically cause intractable peptic ulcer disease (Zollinger-Ellison syndrome), not WDHA syndrome.

**(Choice C)** Ghrelin is produced in the stomach and regulates food intake. Levels increase in fasting states and fall after eating. Ghrelin antagonists are being investigated as drug targets.

**(Choice D)** A glucagonoma is a pancreatic alpha cell tumor that hypersecretes glucagon and can cause secondary diabetes mellitus and necrolytic migratory erythema of the skin.

**(Choice E)** Motilin is produced by the duodenal mucosa and stimulates smooth muscle contraction in the upper GI tract. The antibiotic erythromycin acts as an agonist at motilin receptors in the stomach and duodenum, contributing to the drug's GI side effects.

### Educational objective:

VIPomas are pancreatic islet cell tumors that hypersecrete vasoactive intestinal peptide (VIP), which increases intestinal chloride loss into the stool and causes excess losses of the accompanying water, sodium, and potassium. VIP also inhibits gastric acid secretion. Somatostatin inhibits the secretion of VIP and is used to treat the symptoms of VIPoma.





A 39-year-old woman comes to the emergency department due to several episodes of severe upper abdominal pain. Her pain is triggered by fatty foods and resolves spontaneously. The symptoms first began a few months earlier after an uncomplicated pregnancy. Past medical history is notable for hypertension, for which the patient takes a calcium channel blocker, and hypertriglyceridemia, which is treated with a fibrate. Temperature is 37.2 C (98.9 F) and blood pressure is 143/76 mm Hg. The patient weighs 95 kg (210 lb) and is 173 cm (5 ft 8 in) tall. Ultrasound reveals thickening of the gallbladder wall, with tenderness elicited by the ultrasound probe directly over the gallbladder. She undergoes a laparoscopic cholecystectomy, with multiple stones noted in the contents of the gallbladder. Decreased activity of which of the following enzymes would most likely have contributed to this patient's condition?

- ☐ A. Aromatase
- ☐ B.  $\beta$ -glucuronidase
- ☐ C. Cholesterol 7 $\alpha$ -hydroxylase
- ☐ D. HMG-CoA reductase
- ☐ E. Thiolase



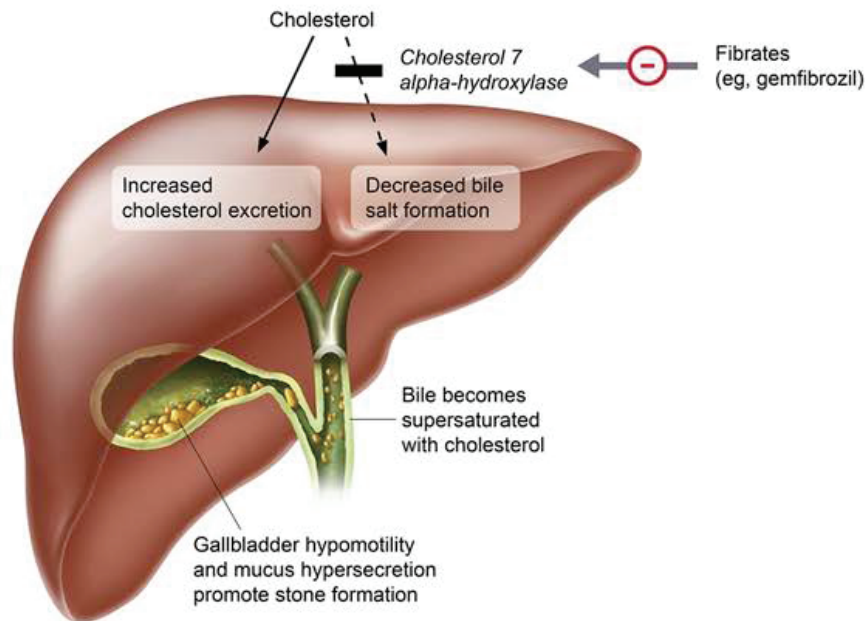
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- ☐ A. Aromatase (3%)
- ☐ B.  $\beta$ -glucuronidase (14%)
- ☒ C. Cholesterol 7 $\alpha$ -hydroxylase (65%)
- ☐ D. HMG-CoA reductase (14%)
- ☐ E. Thiolase (2%)



## Exhibit Display

## Formation of cholesterol gallstones



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This patient, with recurring abdominal pain, a positive "sonographic Murphy sign," and multiple cholesterol **gallstones**, has acute cholecystitis. Water-insoluble **cholesterol** is secreted in bile, where it is solubilized by detergent-like bile salts and phosphatidylcholine. If there is more cholesterol than can be dissolved by the bile salts, it will **precipitate** into insoluble crystals, leading to formation of gallstones. Risk factors for gallstone formation include obesity or rapid weight loss, female sex, glucose intolerance, and hypomotility of the gallbladder (eg, pregnancy, prolonged fasting).

**Fibrate** medications (eg, fenofibrate, gemfibrozil) upregulate lipoprotein lipase, resulting in increased oxidation of fatty acids. In addition, fibrates inhibit **cholesterol 7 $\alpha$ -hydroxylase**, which catalyzes the rate-limiting step in the synthesis of bile acids. The reduced bile acid production results in decreased cholesterol solubility in bile and favors the formation of cholesterol stones.

**(Choice A)** Estrogens increase the biosynthesis of cholesterol by upregulating hepatic HMG-CoA reductase activity. Estrogenic medications (eg, estrogen replacement therapy, combined oral contraceptives) increase the amount of cholesterol secreted in bile and contribute to formation of gallstones. Aromatase catalyzes the conversion of androgens to estrogen; inhibition would lead to reduced gallstone formation.

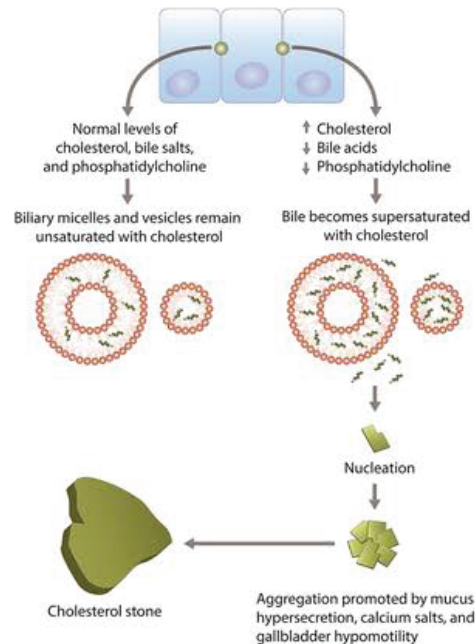
**(Choice B)**  $\beta$ -glucuronidase is released by damaged hepatocytes and bacteria in infected bile. It





## Exhibit Display

## Pathogenesis of cholesterol gallstones







**(Choice B)**  $\beta$ -glucuronidase is released by damaged hepatocytes and bacteria in infected bile. It deconjugates bilirubin, and the resulting free bilirubin precipitates with calcium in the bile to form pigmented gallstones. Decreased activity of this enzyme would reduce the formation of pigmented stones but would not affect the formation of cholesterol gallstones.

**(Choices D and E)** The first step in cholesterol synthesis is the condensation of 2 molecules of acetyl-CoA by acetyl-CoA acetyl transferase (thiolase) to form acetoacetyl-CoA. Condensation with a third molecule of acetyl-CoA yields  $\beta$ -hydroxy- $\beta$ -methylglutaryl-CoA (HMG-CoA). HMG-CoA reductase then catalyzes the conversion of HMG-CoA to mevalonate, the rate-limiting step in cholesterol synthesis. Decreased activity of these enzymes would reduce cholesterol synthesis and the amount of cholesterol secreted in bile, discouraging cholesterol stone formation.

### Educational objective:

Fibrate medications (eg, fenofibrate, gemfibrozil) inhibit cholesterol 7 $\alpha$ -hydroxylase, which catalyzes the rate-limiting step in the synthesis of bile acids. The reduced bile acid production results in decreased cholesterol solubility in bile and favors the formation of cholesterol gallstones.

### References

- [Safety considerations with fibrate therapy.](#)





A 38-year-old woman comes to the office due to intermittent abdominal pain and bloating since childhood. The patient does not drink milk because she does not like the taste and adds, "I eat ice cream, cheese, and yogurt, but they upset my stomach sometimes." There is no associated weight loss, abnormal bleeding, or joint pain. Past medical history is otherwise unremarkable, though the patient has not seen a physician for many years. Vital signs and physical examination are normal. Laboratory studies show normal hemoglobin, iron, and vitamin D levels. A biopsy sample of this patient's small bowel mucosa would most likely show which of the following?

- ☐ A. Atrophy of the intestinal villi
- ☐ B. Collections of neutrophils within crypt lumina
- ☐ C. Distended macrophages in lamina propria
- ☐ D. Infiltration of lamina propria with atypical lymphocytes
- ☐ E. Inflammation with scattered noncaseating granulomas
- ☐ F. Normal intestinal mucosa





The patient does not **drink milk** because she does not like the taste and adds, "I eat ice cream, cheese, and yogurt, but they upset my stomach sometimes." There is no associated weight loss, abnormal bleeding, or joint pain. Past medical history is otherwise unremarkable, though the patient has not seen a physician for many years. Vital signs and physical examination are normal. Laboratory studies show normal hemoglobin, iron, and vitamin D levels. A biopsy sample of this patient's small bowel mucosa would most likely show which of the following?

- ☐ A. Atrophy of the intestinal villi (7%)
- ☐ B. Collections of neutrophils within crypt lumina (1%)
- ☐ C. Distended macrophages in lamina propria (0%)
- ☐ D. Infiltration of lamina propria with atypical lymphocytes (1%)
- ☐ E. Inflammation with scattered noncaseating granulomas (0%)
- ☒ F. Normal intestinal mucosa (87%)

Correct



87%



52 secs



01/05/2021

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This patient, with gastrointestinal distress caused by consumption of lactose-containing dairy products, has typical features of **lactase deficiency**. Lactase deficiency results in incomplete hydrolysis of the disaccharide lactose into glucose and galactose. Undigested lactose in the bowel attracts excess water into the bowel lumen, leading to **osmotic diarrhea**. However, light and electron microscopic examinations show **normal bowel mucosa** in patients with primary lactase deficiency.

Primary lactase deficiency can be classified as congenital or acquired. The congenital variant is a rare autosomal recessive condition that presents with diarrhea after birth. The acquired variant is more common and typically arises from decreased production of lactase by **mid childhood** (lactase nonpersistence).

**(Choices A and E)** Secondary lactase deficiency is seen in disorders that cause injury to the gastrointestinal mucosa. **Celiac disease** is characterized by atrophy of the intestinal villi and is due to exposure to gluten-containing wheat products. Crohn disease causes noncaseating granulomas, and usually presents with abdominal pain and a variety of other gastrointestinal symptoms. Lactase deficiency due to these conditions is usually seen in association with other features of malabsorption (eg, iron deficiency, vitamin D deficiency).

**(Choice B)** Diffuse inflammatory infiltrates with neutrophilic microabscesses in the crypt lumina can be





Item 7 of 40

Question Id: 134



Mark



Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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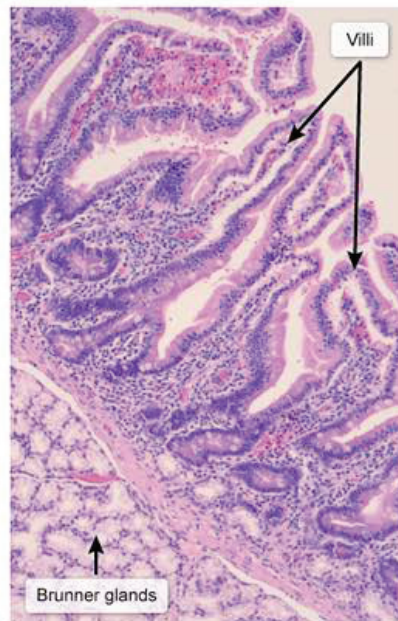
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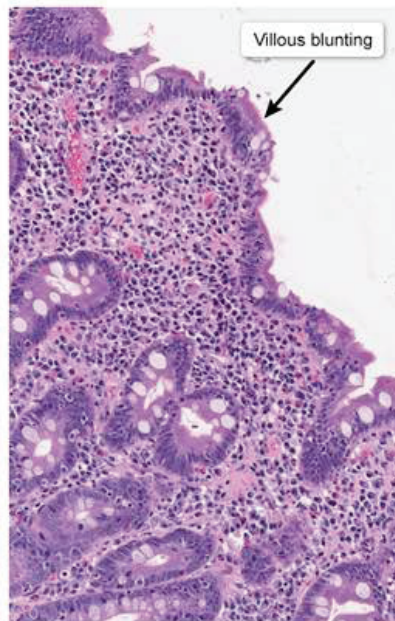
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### Exhibit Display

Normal duodenum



Celiac disease



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Feedback

Suspend

End Block

due to these conditions is usually seen in association with other features or malabsorption (eg, iron deficiency, vitamin D deficiency).

**(Choice B)** Diffuse inflammatory infiltrates with neutrophilic microabscesses in the crypt lumina can be seen in patients with **ulcerative colitis**, which usually presents with intermittent bloody diarrhea and abdominal pain.

**(Choice C)** Distended macrophages in the intestinal lamina propria are a typical finding in **Whipple disease**, which characteristically presents with malabsorptive diarrhea, weight loss, and joint pain.

**(Choice D)** Infiltration of the lamina propria with atypical lymphocytes would be expected in patients with gastrointestinal MALT (mucosa-associated lymphoid tissue) lymphomas. These often occur in the setting of chronic immune stimulation (eg, gastric MALT lymphoma with chronic *Helicobacter pylori* infection).

### Educational objective:

The small bowel mucosa of patients with primary lactase deficiency is normal on histologic examination.

Pathophysiology  
Subject

Gastrointestinal & Nutrition  
System

Lactose intolerance  
Topic

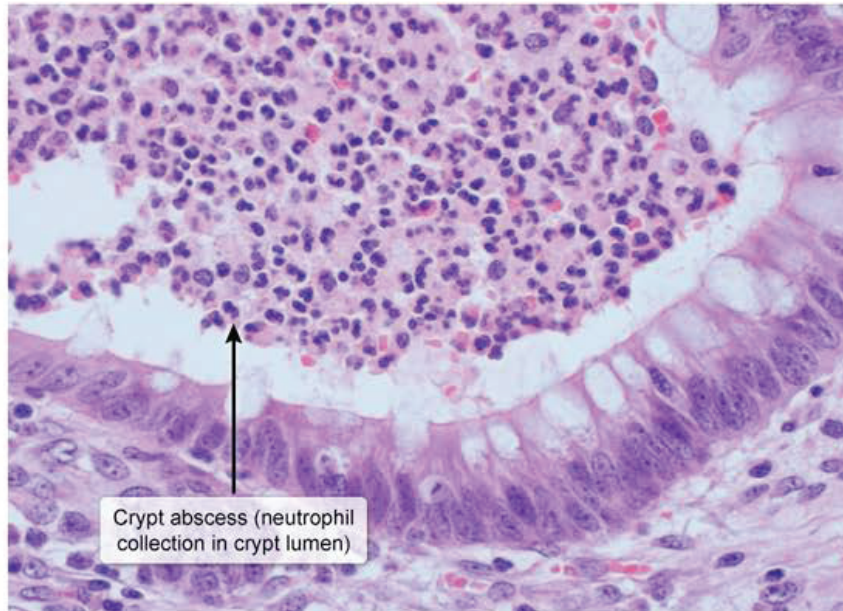
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due to these conditions is usually seen in association with other features of malabsorption (eg, iron

Exhibit Display

Ulcerative colitis



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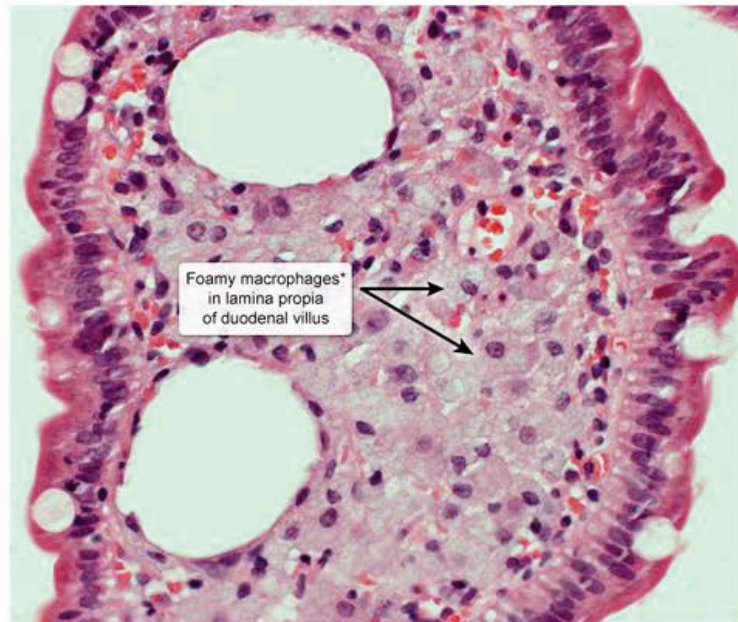
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due to these conditions is usually seen in association with other features of malabsorption (eg, iron

### Exhibit Display

#### Whipple disease



\*Contain Tropheryma whipplei

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A 50-year-old woman comes to the emergency department with severe upper abdominal pain. The pain started suddenly and is sharp and colicky. She has also vomited several times throughout the day, including once while in the emergency department. The patient describes several prior episodes of similar abdominal pain that resolved spontaneously without treatment. Her other medical problems include complicated appendicitis when she was 22 years old. Her temperature is 37.8 C (100 F) and pulse is 112/min. Abdominal examination shows cessation of inspiration with deep palpation of the right upper quadrant. Laboratory assessment shows a serum bilirubin of 0.8 mg/dL and a serum alkaline phosphatase of 100 U/L. Initial imaging studies are equivocal. Which of the following diagnostic test results would be most specific for acute cholecystitis?

- ☐ A. Distended duodenum on upper gastrointestinal series
- ☐ B. Echogenic structures inside the gallbladder on abdominal ultrasound
- ☐ C. Failed gallbladder visualization on radionuclide biliary scan
- ☐ D. Increased serum aspartate and alanine aminotransferase levels
- ☐ E. Opacities in the right subcostal area on abdominal x-ray







started suddenly and is sharp and colicky. She has also vomited several times throughout the day, including once while in the emergency department. The patient describes several prior episodes of similar abdominal pain that resolved spontaneously without treatment. Her other medical problems include complicated appendicitis when she was 22 years old. Her temperature is 37.8 C (100 F) and pulse is 112/min. Abdominal examination shows cessation of inspiration with deep palpation of the right upper quadrant. Laboratory assessment shows a serum bilirubin of 0.8 mg/dL and a serum alkaline phosphatase of 100 U/L. Initial imaging studies are equivocal. Which of the following diagnostic test results would be most specific for acute cholecystitis?

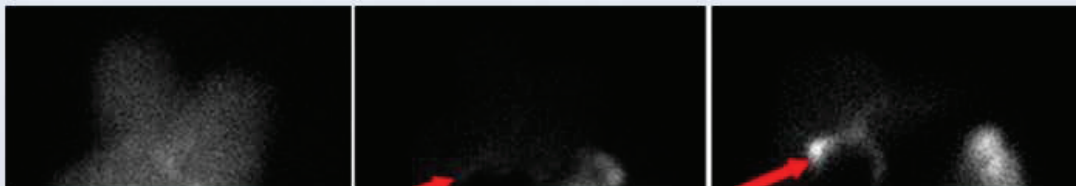
- ☐ A. Distended duodenum on upper gastrointestinal series (2%)
- ☐ B. Echogenic structures inside the gallbladder on abdominal ultrasound (53%)
- ☒ C. Failed gallbladder visualization on radionuclide biliary scan (33%)
- ☐ D. Increased serum aspartate and alanine aminotransferase levels (3%)
- ☐ E. Opacities in the right subcostal area on abdominal x-ray (7%)





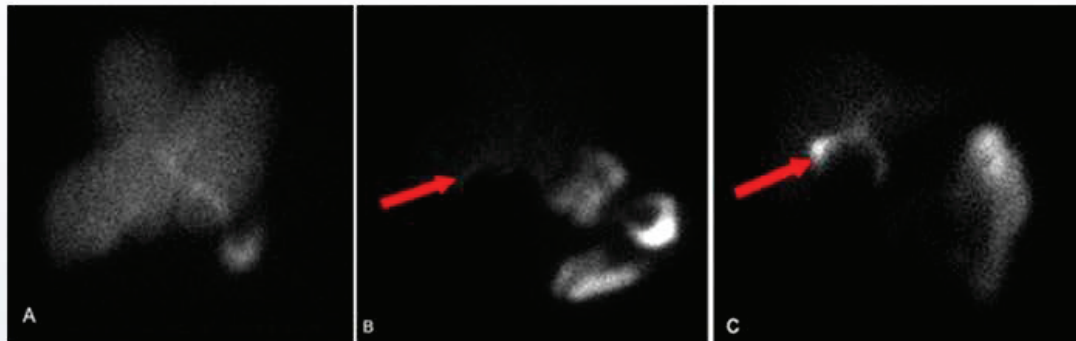
**Acute cholecystitis** is caused by gallstone obstruction of the **cystic duct** in more than 90% of cases. Ingestion of fatty foods then stimulates contraction of the gallbladder against the impacted stone, resulting in severe colicky pain. Mechanical disruption of the gallbladder mucosa and release of inflammatory mediators (eg, lysolecithin, prostaglandins) cause the obstructed gallbladder to become inflamed and edematous. As blood supply to the distended organ becomes compromised, secondary bacterial infection frequently develops. Potential complications include gangrene and perforation, with subsequent formation of a pericholecystic abscess or generalized peritonitis.

Ultrasonography is the **preferred** initial imaging test for the diagnosis of acute cholecystitis; however, nuclear medicine hepatobiliary scanning (ie, cholescintigraphy) can be an alternate means when ultrasonography is **inconclusive**. During a hepatobiliary scan, a radiotracer is administered intravenously and is preferentially taken up by hepatocytes and excreted into bile. Images of the tracer as it moves through the hepatobiliary system and intestine are then obtained for up to several hours after injection.





through the hepatobiliary system and intestine are then obtained for up to several hours after injection.



In patients with a patent cystic duct, the gallbladder will be seen as the radiotracer accumulates and concentrates within (image C). In acute or chronic cholecystitis, the radiotracer will be taken up by the liver with progressive excretion into the common bile duct and proximal small bowel, but the **gallbladder will not be visualized** due to the obstruction (image A and B).

**(Choice A)** Distended duodenum on an upper gastrointestinal series would be suggestive of small-bowel obstruction (as seen with gallstone ileus).

**(Choice B)** The presence of echogenic structures within the gallbladder on ultrasound can be suggestive of acute cholecystitis in the setting of fever and abdominal pain, but it is not diagnostic. Cholelithiasis can







**(Choice B)** The presence of echogenic structures within the gallbladder on ultrasound can be suggestive of acute cholecystitis in the setting of fever and abdominal pain, but it is not diagnostic. Cholelithiasis can also cause more benign biliary colic, or be an incidental asymptomatic finding in the setting of other abdominal pathology. Ultrasound findings more specific for acute cholecystitis include gallbladder wall thickening, pericholecystic fluid, and a positive sonographic Murphy sign.

**(Choice D)** Mild increases in serum aspartate and alanine aminotransferase levels can occur in acute cholecystitis, but they are nonspecific and do not aid the diagnosis.

**(Choice E)** Most patients have insufficient calcium in their gallstones to be visualized on an abdominal x-ray.

### Educational objective:

Acute cholecystitis is most often caused by gallstones obstructing the cystic duct. The diagnosis can be made by identifying signs of gallbladder inflammation (eg, wall thickening, pericholecystic fluid) on ultrasonography. When ultrasound is inconclusive, nuclear medicine hepatobiliary scanning (ie, cholescintigraphy) can be used to assess cystic duct patency and make the diagnosis.

### References

• A systematic review and meta-analysis of diagnostic performance of imaging in acute cholecystitis





A 34-year-old woman comes to the physician with abdominal pain and melena. She also complains of progressive fatigue and a 5 kg (11 lb) weight loss over the last 2 months. She has a strong family history of colon, endometrial, and ovarian cancer. Colonoscopy shows a protuberant, friable mass in the ascending colon, and biopsy is diagnostic for colon adenocarcinoma. Genetic analysis confirms a mutation consistent with Lynch syndrome (hereditary nonpolyposis colon cancer). Which of the following is most likely responsible for the development of colon cancer in this patient?

- ☐ A. Nucleotide mismatches that escape repair
- ☐ B. Covalent bonds between adjacent pyrimidines
- ☐ C. Insertion of abnormal bases (eg, uracil) into DNA
- ☐ D. Empty sugar-phosphate residues in the DNA molecule
- ☐ E. Double-strand breaks in DNA

**Submit**



A 34-year-old woman comes to the physician with abdominal pain and **melena**. She also complains of progressive fatigue and a 5 kg (11 lb) **weight loss** over the last 2 months. She has a strong family history of colon, endometrial, and ovarian cancer. Colonoscopy shows a protuberant, friable mass in the ascending colon, and biopsy is diagnostic for colon **adenocarcinoma**. Genetic analysis confirms a mutation consistent with **Lynch syndrome** (hereditary nonpolyposis colon cancer). Which of the following is most likely responsible for the development of colon cancer in this patient?

- ☒ A. Nucleotide mismatches that escape repair (89%)
- ☐ B. Covalent bonds between adjacent pyrimidines (1%)
- ☐ C. Insertion of abnormal bases (eg, uracil) into DNA (3%)
- ☐ D. Empty sugar-phosphate residues in the DNA molecule (0%)
- ☐ E. Double-strand breaks in DNA (5%)

Correct



89%

Answered correctly



58 secs

Time Spent



12/22/2020

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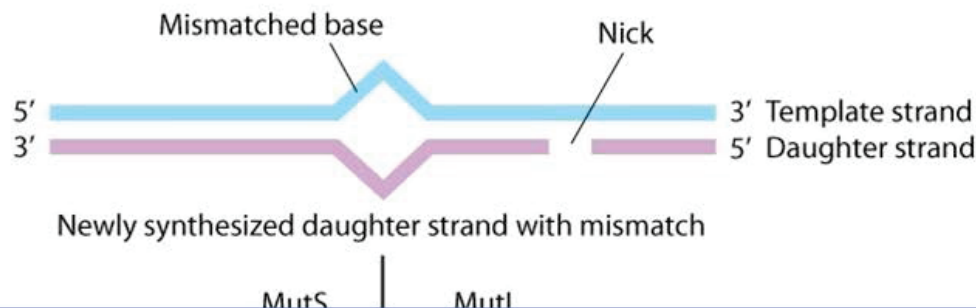
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Lynch syndrome (hereditary nonpolyposis colon cancer) is an autosomal dominant disease caused by defective DNA mismatch repair. DNA replication occurs with a high degree of fidelity because mismatched nucleotides are repaired through the proofreading activity of DNA polymerases delta and epsilon. However, this proofreading functionality is not infallible; base substitutions and small insertion-deletion mismatches occur due to errors in base pairing every  $10^6$  bases on average. It is the function of the DNA mismatch repair system to fix these errors shortly after the daughter strands are synthesized. The mismatch repair system involves several genes, including MSH2 and MLH1, which code for components of the human MutS and MutL homologs. Mutations in these 2 genes account for around 90% of cases of Lynch syndrome.

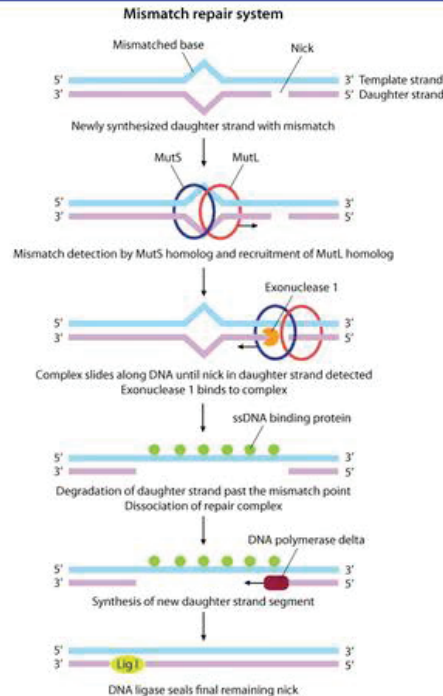
### Mismatch repair system





mismatch repair system involves several genes including MSH2 and MLH1 which code for components of

### Exhibit Display



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## DNA ligase seals final remaining nick

Mismatch repair begins with MutS homolog detecting a mismatch on the newly created daughter strand, which is distinguished from the parent strand by occasional nicks in the phosphodiester bonds. MutL homolog is then recruited, and the resulting complex slides along the DNA molecule until 1 of the daughter strand nicks is encountered. At this point, exonuclease 1 is loaded onto and activated by the repair complex. The daughter strand is then degraded backward past the initial mismatch point, leaving a variable gap of single-stranded DNA that is stabilized by ssDNA-binding protein. The complex then dissociates while DNA polymerase delta loads at the 3' end of the discontinuity and begins synthesizing a new daughter strand segment. Finally, DNA ligase I seals the remaining nick to complete the repair process.

**(Choice B)** Exposure to ultraviolet light can cause pyrimidine (usually thymine) dimers to form due to covalent joining of adjacent pyrimidines. Pyrimidine dimers interfere with DNA replication and are removed by nucleotide excision repair.

**(Choices C and D)** Several types of insults can alter the DNA bases. For example, nitrous acid can deaminate C, A, and G. There are also spontaneous changes, such as deamination of C to U and the constant low-level loss of purines via thermal disruption. Glycosylases are enzymes that detect and





covalent joining of adjacent pyrimidines. Pyrimidine dimers interfere with DNA replication and are removed by nucleotide excision repair.

**(Choices C and D)** Several types of insults can alter the DNA bases. For example, nitrous acid can deaminate C, A, and G. There are also spontaneous changes, such as deamination of C to U and the constant low-level loss of purines via thermal disruption. Glycosylases are enzymes that detect and remove abnormal bases from DNA, creating an empty sugar-phosphate residue that is subsequently removed and replaced by the correct nucleotide (base excision repair).

**(Choice E)** Exposure to ionizing radiation causes double-stranded DNA breaks that are repaired by end-joining repair mechanisms. Non-homologous end joining, the main mechanism in primates, is more prone to cause mutations than homologous recombination.

**Educational objective:**

Lynch syndrome is an autosomal dominant disease caused by abnormal nucleotide mismatch repair. The mismatch repair system involves several genes, including MSH2 and MLH1, which code for components of the human MutS and MutL homologs. Mutations in these 2 genes account for around 90% of cases of Lynch syndrome.

Biochemistry      Gastrointestinal & Nutrition      Lynch syndrome

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A 64-year-old woman is diagnosed with rheumatoid arthritis after coming to the office with symmetrical joint pain, swelling, and morning stiffness. The patient has a remote history of peptic ulcer disease and was treated with multidrug therapy for *Helicobacter pylori* eradication; a follow-up *H pylori* stool antigen test was negative and she had no recurrent symptoms. The patient is started on methotrexate and high-dose ibuprofen therapy. In addition, daily lansoprazole is prescribed for protection against the adverse gastrointestinal effects of ibuprofen. Three months later, joint symptoms were greatly improved. Ibuprofen and lansoprazole were discontinued. However, 2 weeks later, she begins experiencing heartburn after meals. Which of the following is the most likely cause of this patient's new gastrointestinal symptoms?

- ☐ A. Downregulation of vagal stimulation
- ☐ B. Gastrin-mediated rebound acid hypersecretion
- ☒ C. Increased prostaglandin production after ibuprofen discontinuation
- ☐ D. Recolonization with *Helicobacter pylori*
- ☐ E. Upregulation of somatostatin receptors





pain, swelling, and morning stiffness. The patient has a remote history of peptic ulcer disease and was treated with multidrug therapy for *Helicobacter pylori* eradication; a follow-up *H pylori* stool antigen test was negative and she had no recurrent symptoms. The patient is started on methotrexate and high-dose ibuprofen therapy. In addition, daily lansoprazole is prescribed for protection against the adverse gastrointestinal effects of ibuprofen. Three months later, joint symptoms were greatly improved. Ibuprofen and lansoprazole were discontinued. However, 2 weeks later, she begins experiencing heartburn after meals. Which of the following is the most likely cause of this patient's new gastrointestinal symptoms?

- ☐ A. Downregulation of vagal stimulation (1%)
- ☒ B. Gastrin-mediated rebound acid hypersecretion (85%)
- ☐ C. Increased prostaglandin production after ibuprofen discontinuation (6%)
- ☐ D. Recolonization with *Helicobacter pylori* (4%)
- ☐ E. Upregulation of somatostatin receptors (1%)

Correct

85%



01 min, 28 secs



12/29/2020

Block Time Remaining: 00:09:17

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Lab Values



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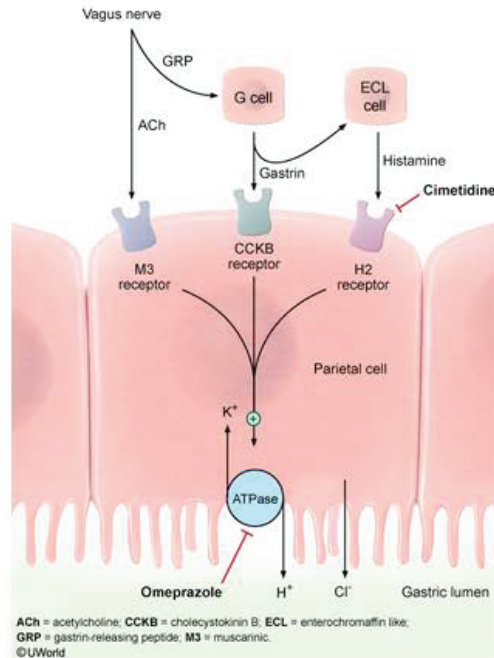


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Vagus nerve

## Exhibit Display

## Parietal cell acid secretion



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GRP = gastrin-releasing peptide; M3 = muscarinic.  
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Release of gastrin, a hormone produced by G cells in the gastric antrum, is stimulated by dietary protein intake, gastrin-releasing peptide (released in response to vagal stimuli), and increased gastric pH. Gastrin induces acid production directly by binding parietal cells and indirectly by binding enterochromaffin-like (ECL) cells and inducing histamine release.

**Proton pump inhibitors** (PPIs) (eg, omeprazole, lansoprazole) inhibit the hydrogen-potassium-ATPase pump and **decrease hydrochloric acid** production regardless of stimuli. The resultant increase in gastric pH leads to **increased gastrin** formation, which induces hypertrophy of the ECL and parietal cells.

**Withdrawal** of the PPI results in overstimulation of the parietal cells with hyperfunctioning of the unblocked ATPase, leading to **rebound gastric acid hypersecretion** and reflux symptoms. PPIs can be slowly tapered to help prevent this adverse effect.

**(Choice A)** Acetylcholine (released with vagal stimulation) binds to parietal cell muscarinic (M3) receptors and promotes the secretion of hydrochloric acid. Downregulation of vagal tone would likely relieve, rather than cause, the patient's symptoms.

**(Choice C)** Prostaglandins decrease acid production by inhibiting the downstream messenger of histamine and increases bicarbonate formation from gastric epithelial cells. Nonsteroidal anti-inflammatory drugs (eg



main cause, the patient's symptoms.

**(Choice C)** Prostaglandins decrease acid production by inhibiting the downstream messenger of histamine and increases bicarbonate formation from gastric epithelial cells. Nonsteroidal anti-inflammatory drugs (eg ibuprofen) inhibit prostaglandin formation and increase the risk of gastritis and peptic ulcer formation. Increased prostaglandin formation after drug withdrawal would be protective against gastritis.

**(Choice D)** Chronic *Helicobacter pylori* infection causes atrophic gastritis with parietal cell destruction. The effects of hypergastrinemia are masked in these patients due to the inability of the remaining parietal cells to create large volumes of acid. Reinfection is very rare, and the correlation with PPI withdrawal makes rebound hypersecretion more likely.

**(Choice E)** Somatostatin inhibits histamine and gastrin release; upregulation would lead to reduced gastric acid formation.

**Educational objective:**

Elevated gastric pH stimulates secretion of gastrin, a polypeptide hormone that increases gastric acid production. Proton pump inhibitors block gastric acid production by parietal cells; the resultant increase in pH leads to hypergastrinemia, which can cause rebound hypersecretion of gastric acid when the drug is withdrawn.





A 54-year-old man is evaluated in the clinic due to generalized weakness and lethargy for the past 5 years. He has no history of hypothyroidism or depression. The patient uses acetaminophen intermittently for joint pains that he attributes to "old age." He drinks alcohol occasionally but does not use tobacco or illicit drugs. His older brother died of liver cirrhosis. Laboratory tests show a serum ferritin level of 1800  $\mu\text{g/L}$ . If this patient's disorder is hereditary, the genetic defect responsible for his condition most likely affects which of the following processes?

- ☐ A. Blood iron transport
- ☐ B. Hemoglobin synthesis
- ☐ C. Hepatic iron excretion
- ☐ D. Intestinal iron absorption
- ☐ E. Renal iron excretion

**Submit**



A 54-year-old man is evaluated in the clinic due to generalized weakness and lethargy for the past 5 years. He has no history of hypothyroidism or depression. The patient uses acetaminophen intermittently for joint pains that he attributes to "old age." He drinks alcohol occasionally but does not use tobacco or illicit drugs. His older brother died of liver cirrhosis. Laboratory tests show a serum ferritin level of 1800  $\mu\text{g/L}$ . If this patient's disorder is hereditary, the genetic defect responsible for his condition most likely affects which of the following processes?

- ☐ A. Blood iron transport (9%)
- ☐ B. Hemoglobin synthesis (3%)
- ☐ C. Hepatic iron excretion (24%)
- ☒ D. Intestinal iron absorption (60%)
- ☐ E. Renal iron excretion (1%)

Correct



60%

Answered correctly



45 secs

Time Spent



09/08/2020

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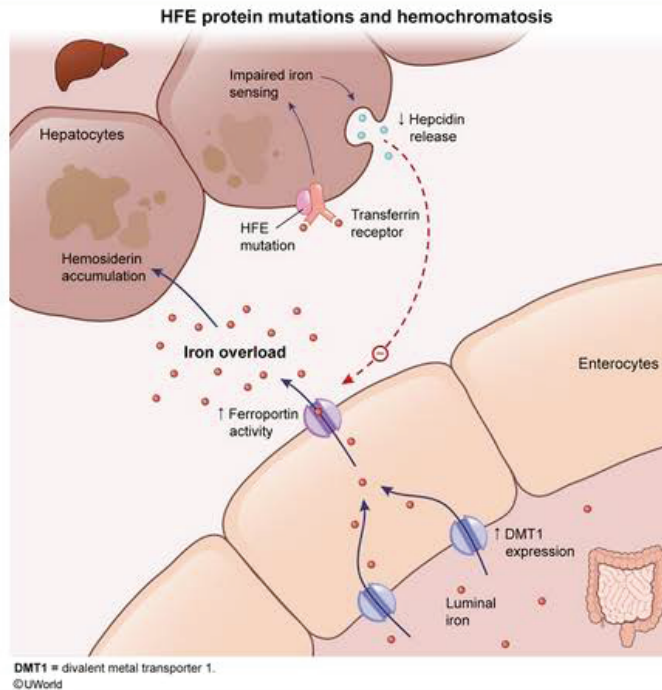
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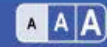
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This patient likely has **hereditary hemochromatosis**, an autosomal recessive disorder characterized by excessive intestinal iron absorption and accumulation within parenchymal tissues that result in end-organ damage (eg, cirrhosis, diabetes mellitus, cardiomyopathy, arthropathy). The condition is frequently caused by a missense mutation in the **HFE gene** (eg, C282Y), which is most commonly found in Caucasians.

The HFE protein interacts with the transferrin receptor on the cell surface to facilitate endocytosis of the iron-transferrin complex. Once inside the cell, transferrin is degraded and the released iron is added to the labile iron pool. Mutation of the HFE protein leads to reduced iron uptake and causes enterocytes and hepatocytes to sense falsely low iron levels. This enhances iron accumulation in the body via 2 mechanisms:

1. Enterocytes increase apical expression of divalent metal transporter 1 (DMT1), **increasing intestinal iron absorption** from the lumen.
2. Hepatocytes **decrease hepcidin** synthesis, which increases ferroportin expression on the basolateral surface of enterocytes and promotes iron secretion into the circulation.

Excessive iron accumulation results in elevated levels of serum ferritin (cellular iron storage protein) and increased saturation of transferrin (major iron transporter in the plasma).





Excessive iron accumulation results in elevated levels of serum ferritin (cellular iron storage protein) and increased saturation of transferrin (major iron transporter in the plasma).

**(Choice A)** Iron transport in the blood is not impaired in hereditary hemochromatosis as transferrin function is normal.

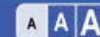
**(Choice B)** Patients with severe forms of thalassemia (eg, beta thalassemia major) often have chronic hemolytic anemia and develop iron overload due to repeated blood transfusions (secondary hemochromatosis). However, hemoglobin production is normal in patients with hereditary hemochromatosis as iron transport to the bone marrow is unaffected.

**(Choices C and E)** Total body iron levels are regulated by varying the rate of intestinal iron absorption. Although iron loss occurs through sloughing of the intestinal lining and during menstruation in women, there are no regulated mechanisms to excrete iron from the body.

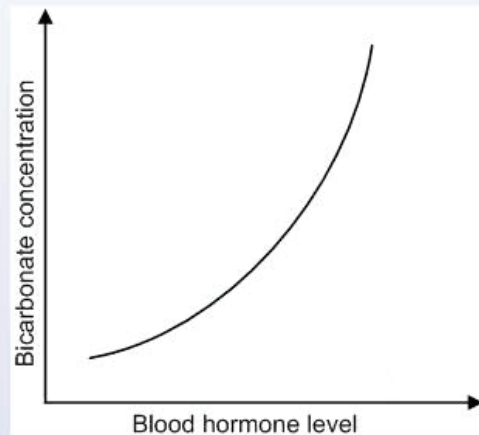
### Educational objective:

Hereditary hemochromatosis is most commonly caused by a missense mutation in the *HFE* gene, resulting in excessive intestinal iron absorption and organ damage (eg, cirrhosis, diabetes mellitus, cardiomyopathy, arthropathy) due to iron accumulation within parenchymal tissues.





A 50-year-old man with a remote history of alcohol dependence is evaluated in the clinic for chronic diarrhea and weight loss. The patient has had bloating with daily loose stools for the past 2 years. His stool is described as greasy and malodorous. Pancreatic insufficiency is suspected despite normal abdominal imaging. The patient undergoes a test in which bicarbonate concentration is measured from duodenal aspirates as hormone A is infused intravenously. The data is plotted in the graph below.



Hormone A is most likely produced by which of the following cell types?



A Duodenal S cells







Previous



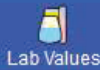
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Full Screen



Tutorial



Lab Values



Notes



Calculator



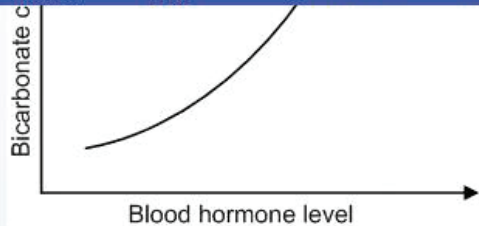
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Hormone A is most likely produced by which of the following cell types?

- ☐ A. Duodenal S cells
- ☐ B. Gastric G cells
- ☐ C. Pancreatic alpha cells
- ☐ D. Pancreatic beta cells
- ☐ E. Parenchymal hepatocytes
- ☐ F. Renal peritubular cells

Submit



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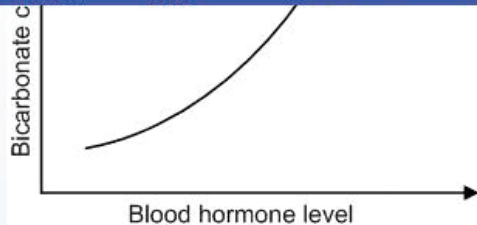
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End Block



Hormone A is most likely produced by which of the following cell types?

- ☒ A. Duodenal S cells (81%)
- ☐ B. Gastric G cells (9%)
- ☐ C. Pancreatic alpha cells (5%)
- ☐ D. Pancreatic beta cells (1%)
- ☐ E. Parenchymal hepatocytes (0%)
- ☐ F. Renal peritubular cells (0%)

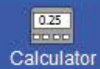
Correct

81%  
Answered correctly

47 secs  
Time spent

12/24/2020  
Last updated





### Important gastrointestinal hormones

Hormone	Actions	Secretion site
Gastrin	<ul style="list-style-type: none"><li>• ↑ Gastric <math>H^+</math> secretion</li></ul>	G cells (gastric antrum, duodenum)
Somatostatin	<ul style="list-style-type: none"><li>• ↓ Secretion of most GI hormones</li></ul>	D cells (pancreatic islets, gut mucosa)
Cholecystikin	<ul style="list-style-type: none"><li>• ↑ Pancreatic enzyme &amp; <math>HCO_3^-</math> secretion</li></ul>	I cells (small intestine)
Secretin	<ul style="list-style-type: none"><li>• ↑ Pancreatic <math>HCO_3^-</math> secretion</li><li>• ↓ Gastric <math>H^+</math> secretion</li></ul>	S cells (small intestine)
GIP	<ul style="list-style-type: none"><li>• ↑ Insulin release</li><li>• ↓ Gastric <math>H^+</math> secretion</li></ul>	K cells (small intestine)
Motilin	<ul style="list-style-type: none"><li>• ↑ GI motility</li></ul>	M cells (small intestine)







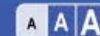
**Secretin** is a hormone produced by **intestinal S cells** that **increases bicarbonate secretion** from the pancreas. Secretin stimulates the **exocrine pancreatic ductal cells** to release a high volume of **bicarbonate-rich and chloride-poor fluid** into the small bowel. The release of gastric acid into the duodenum is the most potent stimulus for secretin release, which begins as the duodenal pH drops below 5 and rises dramatically as the pH drops below 3. The sodium bicarbonate in the pancreatic secretions neutralizes the hydrochloric acid from the gastric contents in a reaction that produces sodium chloride and carbonic acid. Secretin has little to no effect on the secretion of enzymes from pancreatic acinar cells, which is instead under the control of cholecystokinin.

**(Choice B)** Gastrin is the major hormone secreted by G cells of the gastric antrum. Gastrin increases parietal cell acid production and therefore increases the amount of acid delivered from the stomach to the duodenum.

**(Choices C and D)** The endocrine pancreas is composed of glucagon-producing alpha cells, insulin-producing beta cells, and somatostatin-producing D cells. Insulin and glucagon help regulate blood glucose levels and metabolic homeostasis. Somatostatin inhibits the secretion of insulin, glucagon, gastrin, and most other gastrointestinal hormones.

**(Choice E)** The liver parenchyma is not a significant source of circulating hormones that affect pancreatic





glucose levels and metabolic homeostasis. Somatostatin inhibits the secretion of insulin, glucagon, gastrin, and most other gastrointestinal hormones.

**(Choice E)** The liver parenchyma is not a significant source of circulating hormones that affect pancreatic exocrine function.

**(Choice F)** Renal peritubular cells are responsible for producing erythropoietin, a hormone that stimulates red blood cell production in the bone marrow.

### Educational objective:

Secretin is produced by S cells in the duodenal mucosa in response to stimulation by intraluminal acidity. Secretin stimulates the release of bicarbonate-rich secretions from the exocrine pancreas, which is the major source of acid-neutralizing bicarbonate entering the duodenum.

### References

- [Secretin, 100 years later.](#)
- [Neurohormonal control of exocrine pancreas.](#)

Physiology

Gastrointestinal &amp; Nutrition

Gastrointestinal hormones

Subject

System

Topic





A 21-year-old man comes to the emergency department due to abdominal pain, nausea, and vomiting. The patient started having vague periumbilical pain in the morning. Over the next several hours, the pain became more severe, sharper, and localized to the right lower abdominal quadrant. Temperature is 38.3 C (100.9 F), blood pressure is 132/84 mm Hg, pulse is 102/min, and respirations are 12/min. Physical examination shows maximal tenderness in the right lower abdomen two-thirds of the distance from the umbilicus to the anterior superior iliac spine. Bowel sounds are decreased. Laboratory studies reveal a leukocyte count of 16,000/mm<sup>3</sup>. The change in this patient's pain characteristics is most likely explained by which of the following?

- ☐ A. Involvement of the obturator internus muscle
- ☐ B. Inflammation of the psoas major muscle
- ☐ C. Stimulation of the cecal nerve endings
- ☐ D. Irritation of the parietal peritoneum
- ☐ E. Retrocecal orientation of the appendix







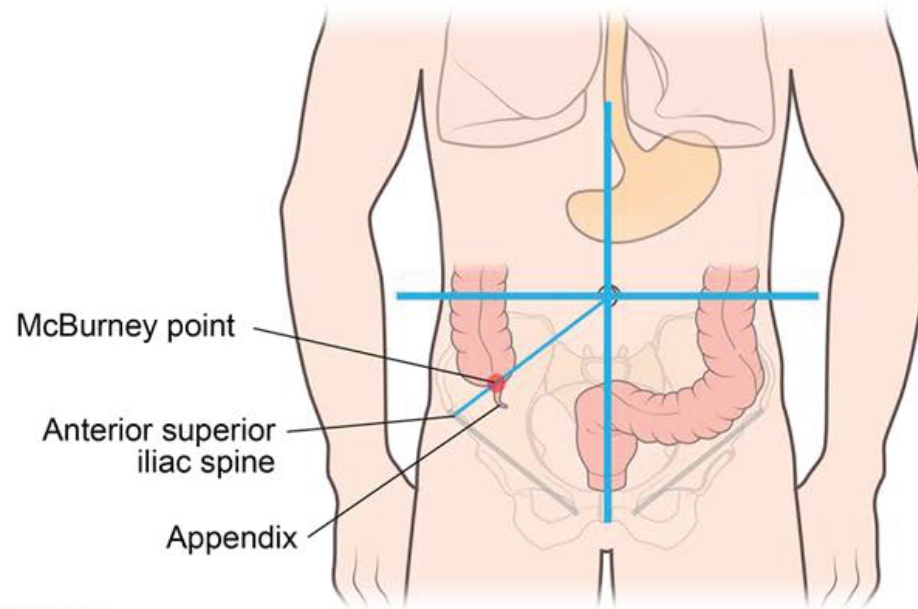
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- ☐ A. Involvement of the obturator internus muscle (1%)
- ☐ B. Inflammation of the psoas major muscle (8%)
- ☐ C. Stimulation of the cecal nerve endings (7%)
- ☒ D. Irritation of the parietal peritoneum (69%)
- ☐ E. Retrocecal orientation of the appendix (13%)



### Exhibit Display

## McBurney point



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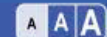
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This patient's presentation is concerning for **appendicitis**, which can cause both visceral (vague, nonlocalized) and somatic (sharp, well-localized) abdominal pain. **Visceral abdominal pain** is most often due to luminal distension and stretching of smooth muscle and is carried by general visceral afferent fibers of the autonomic nervous system. The pain typically occurs in the **midline** region and is **poorly localized** and of a dull, constant, or cramping quality. Patients with visceral pain also commonly develop nausea, vomiting, or sweating due to activation of the autonomic nervous system. In contrast, somatic pain is usually due to irritation of the parietal peritoneum and is well localized, more severe, and worsened with deep inspiration or pushing on the abdominal wall.

The afferent pain fibers for the appendix, proximal colon (including the cecum), and overlying visceral peritoneum cross through the superior mesenteric plexus and enter the spinal cord at the T10 level to produce vague, referred pain at the umbilicus (**Choice C**). As the appendix becomes more inflamed, it irritates the **parietal peritoneum** and abdominal wall and causes a **more severe somatic pain** that **shifts** from the umbilical region to the **McBurney point** (two-thirds of the distance from the umbilicus to the anterior superior iliac spine). With peritoneal irritation, the abdominal wall becomes very sensitive to gentle palpation or sudden release of pressure (ie, rebound tenderness).

The appendix is usually located 2 cm beneath the ileocecal valve in the right lower quadrant. Depending on its orientation, there can be additional clinical findings. A pelvic appendix lies against the right obturator







palpation or sudden release of pressure (ie, rebound tenderness).

The appendix is usually located 2 cm beneath the ileocecal valve in the right lower quadrant. Depending on its orientation, there can be additional clinical findings. A pelvic appendix lies against the right obturator internus muscle, causing right lower quadrant pain with internal rotation of the right hip **(Choice A)**.

Patients with a retrocecal appendix may not have significant right lower quadrant tenderness because the inflamed appendix does not contact the anterior parietal peritoneum, and the cecum (distended with gas) acts as a cushion that blocks the examiner's hand. However, the inflamed appendix will lie against the right psoas muscle, causing pain with hip extension **(Choices B and E)**.

### Educational objective:

Appendicitis causes dull visceral pain at the umbilicus due to afferent pain fibers entering at the T10 level in the spinal cord. Progressive inflammation in the appendix irritates the parietal peritoneum and abdominal wall to cause more severe somatic pain shifting from the umbilicus to McBurney's point (two-thirds of the distance from the umbilicus to the anterior superior iliac spine).

Anatomy

Subject

Gastrointestinal &amp; Nutrition

System

Appendicitis

Topic

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A 45-year-old woman diagnosed with Crohn disease 3 years ago comes to the office due to recurrent right upper quadrant abdominal pain. The pain is graded 5/10 in intensity, is characterized as dull, and occasionally radiates to the right shoulder. It typically occurs after eating fatty meals and is associated with nausea. The patient has no fever, vomiting, melena, or hematochezia. She currently takes infliximab for Crohn disease and atorvastatin for hyperlipidemia. Vital signs and abdominal examination are normal. Abdominal ultrasonography reveals multiple mobile calculi within the gallbladder. Which of the following processes is most likely responsible for the development of gallstones in this patient?

- ☐ A. Gallbladder hypomobility
- ☐ B. Increased bile acid wasting
- ☐ C. Increased intestinal oxalate absorption
- ☐ D. Medication side effect
- ☐ E. Red blood cell destruction

**Submit**



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- ☐ D. Medication side effect
- ☐ E. Red blood cell destruction

**Submit**





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- ☐ A. Gallbladder hypomobility (18%)
- ☒ B. Increased bile acid wasting (45%)
- ☐ C. Increased intestinal oxalate absorption (16%)
- ☐ D. Medication side effect (18%)
- ☐ E. Red blood cell destruction (1%)





Item 14 of 40

Question Id: 412



Mark



Previous



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Tutorial



Lab Values



Notes



Calculator



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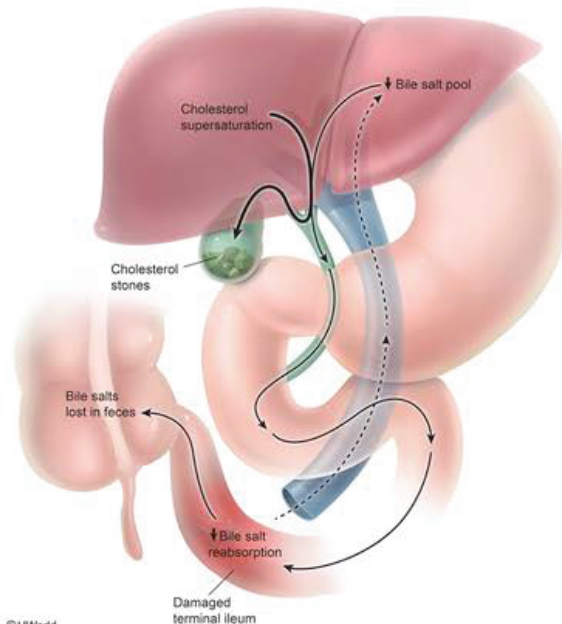


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## Exhibit Display

Pathogenesis of gallstones  
in Crohn disease

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terminal ileum

This patient with Crohn disease most likely developed gallstones due to inflammation of the terminal ileum causing decreased bile acid reabsorption.

**Bile acids** are produced in the liver and excreted with bile into the duodenum. There, they **emulsify fat droplets** to form water-soluble micelles that allow pancreatic lipase to efficiently hydrolyze triglycerides into fatty acids and monoglycerides. In the jejunum, these micelles come in close contact with the gut epithelium, which facilitates the passive absorption of fatty acids, monoglycerides, and cholesterol across the brush border into enterocytes. However, bile acids are ionized molecules that cannot passively cross the intestinal wall. The bile acids eventually reach the **terminal ileum**, where specialized transport proteins allow them to be **reabsorbed**.

The terminal ileum is a typical location of activity in **Crohn disease**. When the mucosa of the terminal ileum is inflamed, **bile acids are lost in the feces**. As a result, a lesser amount of bile acid is present in the bile, so the ratio of cholesterol/bile acids increases. Supersaturation of the bile with cholesterol then leads to formation of **gallstones**.

**(Choice A)** Gallbladder hypomotility may contribute to cholesterol gallstone formation in patients with spinal cord injury or those receiving total parenteral nutrition; however, this is not observed with Crohn





leads to formation of **gallstones**.

**(Choice A)** Gallbladder hypomotility may contribute to cholesterol gallstone formation in patients with spinal cord injury or those receiving total parenteral nutrition; however, this is not observed with Crohn disease.

**(Choice C)** Increased intestinal oxalate absorption can contribute to calcium oxalate **kidney** stone formation in patients with Crohn disease (enteric oxaluria). However, this process is not responsible for the development of gallstones.

**(Choice D)** Statins inhibit the rate-limiting step of cholesterol synthesis (HMG-CoA reductase), which reduces the risk of gallstone formation. Infliximab is a tumor necrosis factor-alpha inhibitor used to treat severe or refractory Crohn disease; it is associated with an increased risk of serious infections.

**(Choice E)** Chronic hemolytic anemias are associated with the development of pigment gallstones due to the increased secretion of bilirubin into bile. Crohn disease can cause anemia due to nutrient deficiency (eg, vitamin B<sub>12</sub>, iron) and chronic inflammation (eg, anemia of chronic disease), but it does not typically cause hemolysis.

**Educational objective:**

Patients with Crohn disease affecting the terminal ileum (most common site of involvement) are prone to



development of gallstones.

**(Choice D)** Statins inhibit the rate-limiting step of cholesterol synthesis (HMG-CoA reductase), which reduces the risk of gallstone formation. Infliximab is a tumor necrosis factor-alpha inhibitor used to treat severe or refractory Crohn disease; it is associated with an increased risk of serious infections.

**(Choice E)** Chronic hemolytic anemias are associated with the development of pigment gallstones due to the increased secretion of bilirubin into bile. Crohn disease can cause anemia due to nutrient deficiency (eg, vitamin B<sub>12</sub>, iron) and chronic inflammation (eg, anemia of chronic disease), but it does not typically cause hemolysis.

### Educational objective:

Patients with Crohn disease affecting the terminal ileum (most common site of involvement) are prone to developing gallstones. Decreased bile acid reabsorption by the inflamed terminal ileum promotes cholesterol supersaturation of the bile, resulting in gallstone formation.

### References

- [Pathogenesis of gall stones in Crohn's disease: an alternative explanation.](#)
- [Gallbladder bile composition in patients with Crohn's disease.](#)





A 56-year-old man comes to the physician complaining of early satiety, nausea, and vague epigastric pain for the past 4 months. He has a 36-pack-year smoking history and admits to drinking alcohol daily for the past 15 years. On physical examination, the patient appears thin and cachectic. Palpation of his abdomen reveals splenomegaly. Abdominal CT scan shows a large irregular mass extending posteriorly from the greater curvature of the stomach, impinging on the splenic artery and vein as they pass below. Tissues supplied by which of the following arteries would most likely be affected by compression of the splenic artery?

- ☐ A. Gastroduodenal
- ☐ B. Left gastroepiploic
- ☐ C. Right gastric
- ☐ D. Right gastroepiploic
- ☐ E. Short gastric

**Submit**





A 56-year-old man comes to the physician complaining of early satiety, nausea, and vague epigastric pain for the past 4 months. He has a 36-pack-year smoking history and admits to drinking alcohol daily for the past 15 years. On physical examination, the patient appears thin and cachectic. Palpation of his abdomen reveals splenomegaly. Abdominal CT scan shows a large irregular mass extending posteriorly from the greater curvature of the stomach, impinging on the splenic artery and vein as they pass below. Tissues supplied by which of the following arteries would most likely be affected by compression of the splenic artery?

- ☐ A. Gastroduodenal (4%)
- ☐ B. Left gastroepiploic (31%)
- ☐ C. Right gastric (4%)
- ☐ D. Right gastroepiploic (5%)
- ☒ E. Short gastric (54%)





Item 15 of 40

Question Id: 8574



Mark



Previous



Next



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Tutorial



Lab Values



Notes



Calculator



Reverse Color



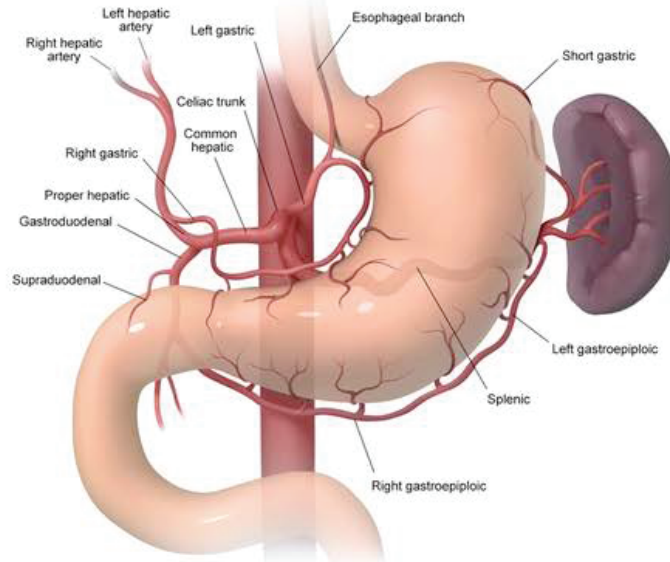
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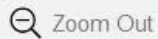
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### Exhibit Display

#### Upper abdominal vasculature



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Left gastroepiploic

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The splenic artery originates from the celiac artery and courses superior to the pancreas. Along its route, it gives off **several branches** to the stomach and pancreas before reaching the spleen. The short gastric arteries and the left gastroepiploic artery arise from the splenic artery immediately after it passes the greater curvature of the stomach. The short gastric arteries have very poor anastomoses, and the tissue supplied by them is vulnerable to ischemic injury following splenic artery blockage. In contrast, tissues supplied by the left gastroepiploic artery can be alternatively supplemented by its strong anastomotic connection with the right gastroepiploic artery **(Choice B)**.

**(Choice A)** The gastroduodenal artery supplies blood to the pylorus and the proximal part of the duodenum. It arises from the common hepatic artery.

**(Choice C)** The right gastric artery supplies blood to the distal lesser curvature of the stomach. It arises from the proper hepatic artery.

**(Choice D)** The right gastroepiploic artery arises from the gastroduodenal artery and perfuses the distal greater curvature of the stomach. It forms an anastomosis with the left gastroepiploic artery.

### Educational objective:

The splenic artery originates from the **celiac artery** and gives off several branches to the stomach and







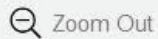
Exhibit Display

Splenic artery branches	Distribution
Pancreatic branches	Run posterior to the upper border of the pancreas, supplying its body and tail
Left gastroepiploic artery	Supply the middle part of the greater curvature of the stomach
Short gastric branches	Supplies the upper part of the greater curvature of the stomach

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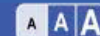


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supplied by the left gastroepiploic artery can be alternatively supplemented by its strong anastomotic connection with the right gastroepiploic artery (**Choice B**).

**(Choice A)** The gastroduodenal artery supplies blood to the pylorus and the proximal part of the duodenum. It arises from the common hepatic artery.

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**(Choice D)** The right gastroepiploic artery arises from the gastroduodenal artery and perfuses the distal greater curvature of the stomach. It forms an anastomosis with the left gastroepiploic artery.

### Educational objective:

The splenic artery originates from the **celiac artery** and gives off several branches to the stomach and pancreas (pancreatic, short gastric, and left gastroepiploic arteries) before finally reaching the spleen. Due to poor anastomoses, the gastric tissue supplied by the short gastric arteries is vulnerable to ischemic injury following splenic artery blockage.

Anatomy

Gastrointestinal &amp; Nutrition

Gastrointestinal blood supply

Subject

System

Topic





A 57-year-old woman is hospitalized with high-grade fevers, chills, and right upper abdominal pain. The patient lives in Wisconsin and has no history of international travel. Her temperature is 40 C (104 F). Physical examination of the abdomen shows rebound tenderness. Laboratory studies show elevated aspartate and alanine aminotransferases. Imaging studies reveal a fluid-filled cavity within the right lobe of the liver as shown below.







Item 16 of 40

Question Id: 62



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Reverse Color



Text Zoom



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### Exhibit Display



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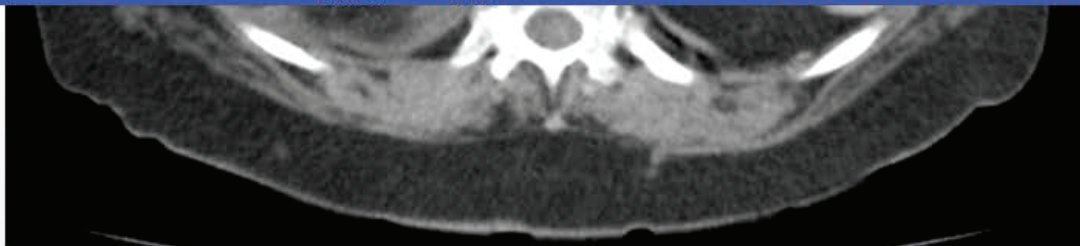
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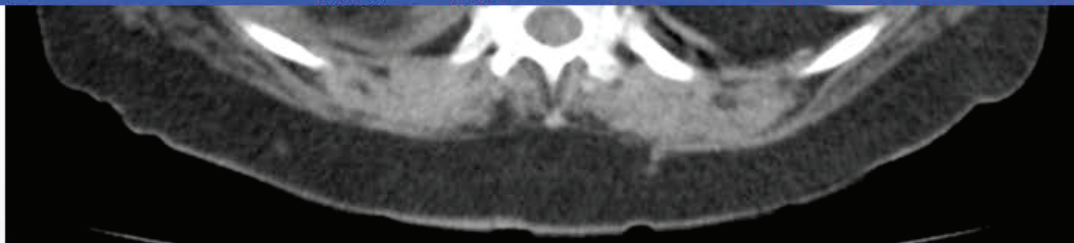


Which of the following microorganism/route combinations is most likely to be the cause of this patient's infection?

- ☐ A. *Chlamydia trachomatis* due to ascending cholangitis
- ☐ B. Cytomegalovirus by direct invasion from a nearby source
- ☐ C. *Entamoeba histolytica* due to a penetrating stab wound
- ☐ D. *Staphylococcus aureus* by hematogenous route
- ☐ E. *Streptococcus pneumoniae* by portal vein

Submit





Which of the following microorganism/route combinations is most likely to be the cause of this patient's infection?

- ☐ A. *Chlamydia trachomatis* due to ascending cholangitis (7%)
- ☐ B. Cytomegalovirus by direct invasion from a nearby source (6%)
- ☐ C. *Entamoeba histolytica* due to a penetrating stab wound (37%)
- ☒ D. *Staphylococcus aureus* by hematogenous route (43%)
- ☐ E. *Streptococcus pneumoniae* by portal vein (5%)

Correct

43%  
Answered correctly

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Last updated

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Item 16 of 40

Question Id: 62



Mark



Previous



Next



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Tutorial



Lab Values



Notes



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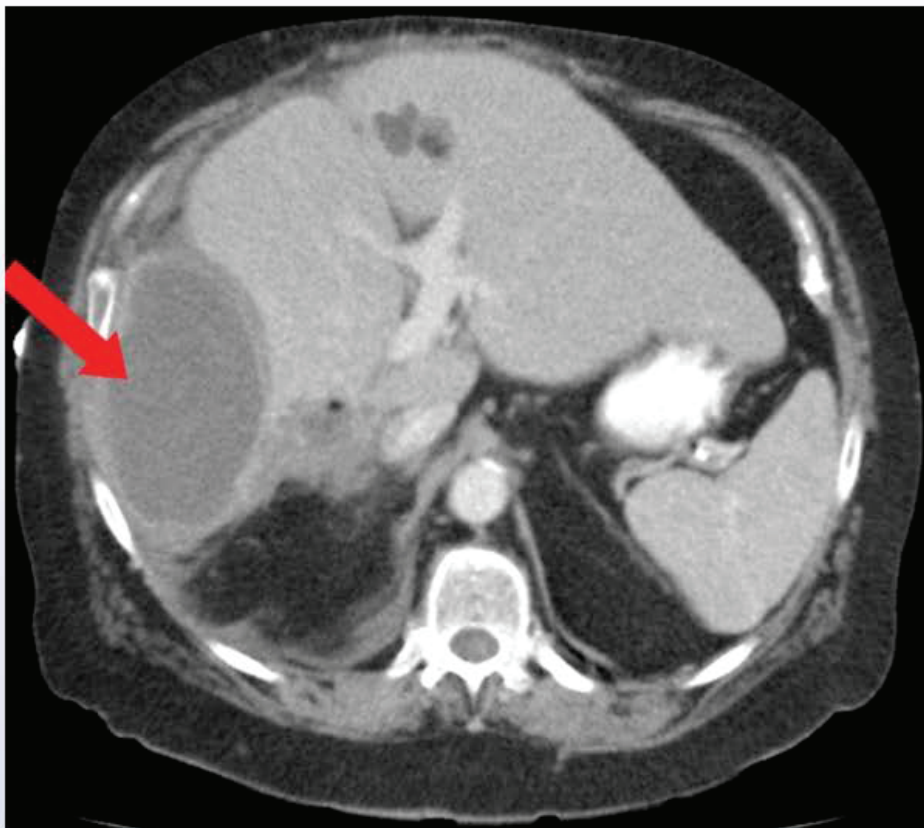
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The presence of a **fluid-filled cavity** in the liver in conjunction with fevers, chills, and right upper abdominal pain is suggestive of a **hepatic abscess**. In developing countries, hepatic abscesses have a relatively high incidence and are usually caused by parasitic infections (eg, *Entamoeba histolytica*, echinococcal). In contrast, hepatic abscesses are uncommon in the United States and are caused by **bacterial infection** in about 80% of cases.

Pyogenic bacteria can gain access to the liver through the following routes:

- **Biliary tract infection** (eg, ascending cholangitis)
- **Portal vein pyemia** (bowel or peritoneal sources)
- Hepatic artery (systemic hematogenous seeding)
- Direct invasion from an adjacent source (eg, peritonitis, cholecystitis)
- Penetrating trauma or injury

The types of organisms causing a hepatic abscess depend on the route of hepatic access. Systemic **hematogenous seeding** of the liver secondary to ***Staphylococcus aureus*** infection at a distant site is the most plausible choice of all the answer options.

**(Choice A)** Ascending cholangitis is usually caused by enteric gram-negative bacilli (eg, *Escherichia coli*,





**(Choice A)** Ascending cholangitis is usually caused by enteric gram-negative bacilli (eg, *Escherichia coli*, *Klebsiella*) and enterococci. *Chlamydia trachomatis* is transmitted sexually and is not found in the enteric environment.

**(Choice B)** Hepatic abscesses that arise by direct invasion from a nearby source are usually enteric gram-negative bacilli and enterococci. Cytomegalovirus can cause hepatitis in the immunosuppressed patient, but it is not associated with the development of a hepatic abscess.

**(Choice C)** Traumatic penetrating injuries to the abdomen (eg, stab wound) typically result in abscesses that contain mixed aerobic and anaerobic flora. *Entamoeba histolytica* is most often transmitted through foodborne exposure and in areas with poor sanitation. It can cause a hepatic abscess by ascending from the colon through the portal venous system.

**(Choice E)** *Streptococcus pneumoniae* colonizes the nasopharynx and typically causes disease within the respiratory tract region (eg, pneumonia, otitis media, sinusitis) and meningitis. However, hepatic abscesses due to portal vein seeding typically arise from abdominal infectious processes (eg, appendicitis, diverticulitis) and *S pneumoniae* is not an enteric pathogen.

**Educational objective:**

*Staphylococcus aureus* can cause hepatic abscesses via hematogenous seeding of the liver. Enteric







**(Choice C)** Traumatic penetrating injuries to the abdomen (eg, stab wound) typically result in abscesses that contain mixed aerobic and anaerobic flora. *Entamoeba histolytica* is most often transmitted through foodborne exposure and in areas with poor sanitation. It can cause a hepatic abscess by ascending from the colon through the portal venous system.

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### Educational objective:

*Staphylococcus aureus* can cause hepatic abscesses via hematogenous seeding of the liver. Enteric bacteria (eg, *Escherichia coli*, *Klebsiella*, and enterococci) can cause hepatic abscesses by ascending the biliary tract (ie, ascending cholangitis), portal vein pyemia, or direct invasion from an adjacent area (eg, cholecystitis).

Microbiology

Gastrointestinal &amp; Nutrition

Liver abscess

Subject

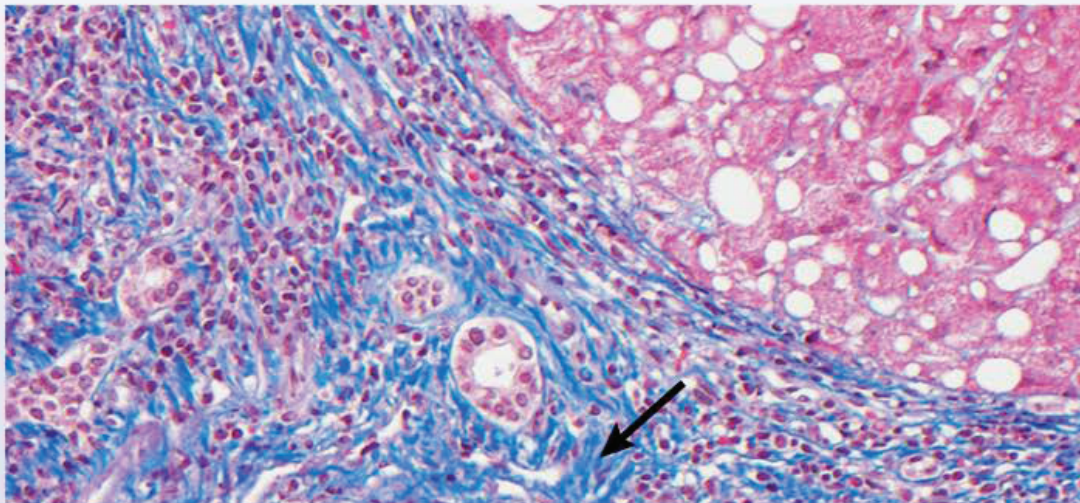
System

Topic





A 62-year-old man comes to the office for the evaluation of jaundice. Medical history is significant for uncontrolled type 2 diabetes mellitus and morbid obesity. He does not use tobacco, alcohol, or illicit drugs. There is no family history of liver disease. Vital signs are within normal limits. BMI is 47 kg/m<sup>2</sup>. Mild scleral icterus is present. Heart and lung sounds are normal. The abdomen is nontender and nondistended. Trace bilateral lower extremity edema is present. Laboratory studies reveal elevated transaminases. A liver biopsy is obtained, and trichrome staining shows the following:







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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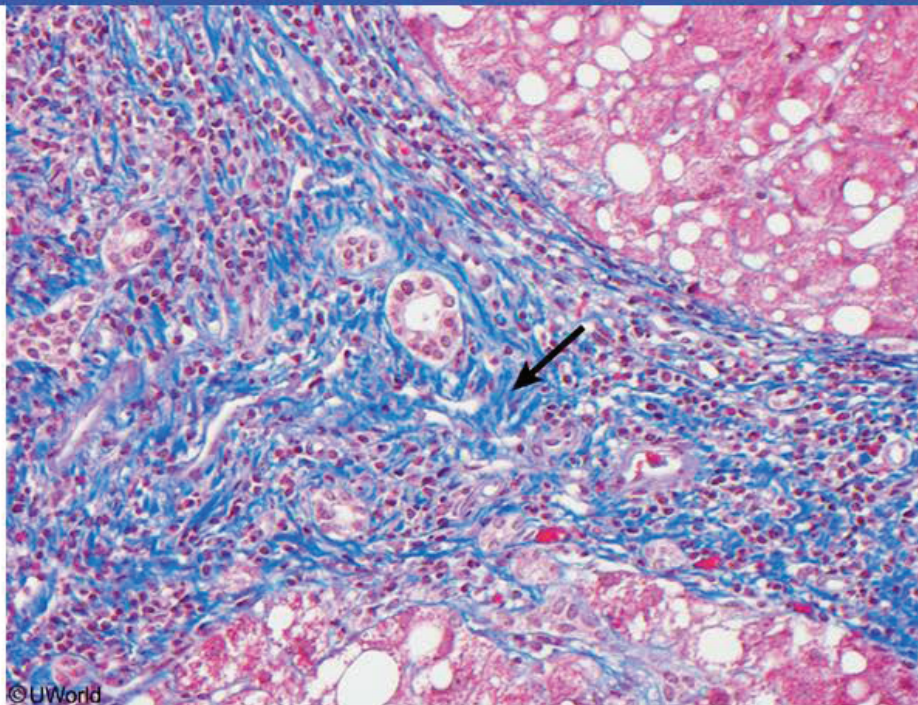


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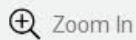


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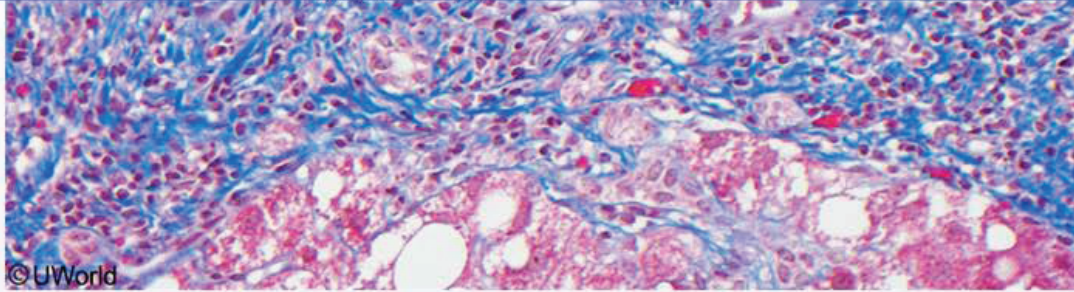


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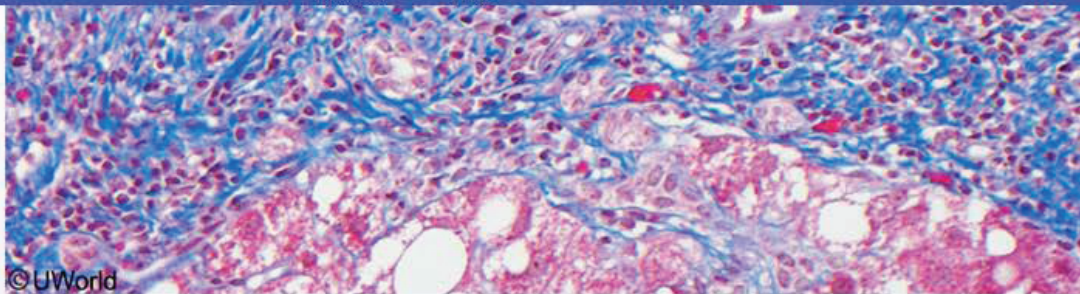




Which of the following cells is directly responsible for the histologic finding indicated by the arrow?

- ☐ A. Cholangiocytes
- ☐ B. Hepatocytes
- ☐ C. Kupffer cells
- ☐ D. Sinusoidal endothelial cells
- ☐ E. Stellate (Ito) cells

Submit



Which of the following cells is directly responsible for the histologic finding indicated by the arrow?

- ☐ A. Cholangiocytes (2%)
- ☐ B. Hepatocytes (5%)
- ☐ C. Kupffer cells (21%)
- ☐ D. Sinusoidal endothelial cells (9%)
- ☒ E. Stellate (Ito) cells (60%)

Correct

60%

15 secs

11/04/2020





## Explanation

### Primary cells of the liver

Cell type	Function
<b>Cholangiocyte</b>	<ul style="list-style-type: none"><li>• Bile duct epithelial cell</li><li>• Transports solutes and electrolytes into bile</li></ul>
<b>Hepatocyte</b>	<ul style="list-style-type: none"><li>• Protein, cholesterol &amp; bile synthesis, gluconeogenesis</li><li>• Drug and fatty acid metabolism</li></ul>
<b>Kupffer cell</b>	<ul style="list-style-type: none"><li>• Macrophages within hepatic sinusoids</li><li>• Phagocytosis of bacteria and RBCs</li></ul>
<b>Stellate cell</b>	<ul style="list-style-type: none"><li>• Quiescent phase: vitamin A storage</li><li>• Activated phase: transform into myofibroblast to secrete collagen (primary cell involved in hepatic fibrosis)</li></ul>

**RBC** = red blood cell.





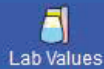
RBC = red blood cell.

This patient with diabetes mellitus and morbid obesity has **hepatic cirrhosis**, likely due to long-standing nonalcoholic fatty liver disease (NAFLD). Cirrhosis is the end stage of multiple liver diseases and is characterized by replacement of normal lobular architecture with regenerating nodules separated by bridging fibrous septae.

Cirrhosis can be visualized histologically as **thickened collagenous bands** (which stain blue with Masson trichrome stain) separating clusters of hepatocytes. Fat infiltration (ie, hepatic steatosis, visible as clear vacuoles within the parenchyma) is commonly seen in both alcoholic fatty liver disease and NAFLD. In response to chronic injury, **stellate (Ito) cells** are activated and transform into **myofibroblasts** capable of proliferating, promoting chemotaxis, and **producing collagen** in large quantities. This leads to progressive scar formation and cirrhosis.

Manifestations of cirrhosis include jaundice, scleral icterus, spider angiomas, and elevated liver enzymes. Evidence of abnormal hepatic synthetic function (eg, abnormal coagulation parameters, hypoalbuminemia) and thrombocytopenia are also common.

**(Choice A)** Cholangiocytes are epithelial cells within the bile duct system. They transport ions and solutes into bile as it travels through the canaliculi.



**(Choice A)** Cholangiocytes are epithelial cells within the bile duct system. They transport ions and solutes into bile as it travels through the canaliculi.

**(Choice B)** Hepatocytes are located in the liver parenchyma and have many functions, including protein synthesis and storage, fatty acid metabolism, gluconeogenesis, cholesterol synthesis, and drug metabolism.

**(Choice C)** Kupffer cells are macrophages that reside within hepatic sinusoids. They are indirectly involved in fibrogenesis because they generate cytokines (ie, TNF-alpha) to assist in the activation of stellate cells; however, their primary function is bacterial phagocytosis and the clearance of red blood cells.

**(Choice D)** Sinusoidal endothelial cells, which line hepatic sinusoids, are fenestrated cells that filter solutes out of the blood and into hepatocytes. They assist in the removal of metabolic waste and other macromolecules from circulation.

**Educational objective:**

Stellate (Ito) cells are the primary cells involved in hepatic fibrosis. In response to hepatic injury, the stellate cells are activated and transform into myofibroblasts capable of proliferating, promoting chemotaxis, and producing large quantities of collagen. Collagen stains blue with Masson trichrome stain.





A 73-year-old man comes to the clinic with epigastric pain that starts 30-40 minutes after meals and does not respond to antacids. The pain is non-radiating and is graded 6/10 in intensity. The patient has lost more than 4.5 kg (10 lb) over the last few months, which he attributes to eating less due to his fear of the pain. He has no vomiting, diarrhea, or urinary symptoms. His past medical history is significant for hypertension, hyperlipidemia, coronary artery bypass grafting, and right-sided carotid endarterectomy. He has smoked a pack of cigarettes daily for 32 years. Upper gastrointestinal endoscopy shows no abnormalities. The underlying pathophysiology of this patient's disease process is most similar to which of the following conditions?

- ☐ A. Aortic dissection
- ☐ B. Diffuse esophageal spasm
- ☐ C. Peptic ulcer disease
- ☐ D. Pulmonary embolism
- ☐ E. Stable angina







not respond to antacids. The pain is non-radiating and is graded 6/10 in intensity. The patient has lost more than 4.5 kg (10 lb) over the last few months, which he attributes to eating less due to his fear of the pain. He has no vomiting, diarrhea, or urinary symptoms. His past medical history is significant for hypertension, hyperlipidemia, coronary artery bypass grafting, and right-sided carotid endarterectomy. He has smoked a pack of cigarettes daily for 32 years. Upper gastrointestinal endoscopy shows no abnormalities. The underlying pathophysiology of this patient's disease process is most similar to which of the following conditions?

- ☐ A. Aortic dissection (2%)
- ☐ B. Diffuse esophageal spasm (9%)
- ☐ C. Peptic ulcer disease (35%)
- ☐ D. Pulmonary embolism (3%)
- ☒ E. Stable angina (49%)

Correct

49%



47 secs



02/01/2021

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This patient's **postprandial epigastric pain** and associated **food aversion/weight loss** in the setting of generalized atherosclerosis (eg, coronary and carotid artery disease) is consistent with **chronic mesenteric ischemia**.

When atherosclerosis involves the mesenteric arteries, the bowel can suffer from **diminished blood supply**. Intestinal hypoperfusion, which can be very painful, is especially pronounced within an hour after meals when more blood is needed for the digestion/absorption of nutrients (intestinal angina). This is **analogous to stable cardiac angina**, chest pain that occurs with physical exertion due to increased myocardial oxygen demand. The diagnosis can be made with duplex ultrasonography or angiography showing high-grade stenosis in the celiac and mesenteric arteries.

**(Choice A)** Aortic dissection results from an aortic intimal tear with formation of a false lumen that can propagate and obstruct the vessels branching off the aorta (eg, renal, splanchnic, spinal, lower limb). A similar process would be more likely to cause acute end-organ damage (eg, cerebral infarction) rather than chronic, episodic ischemia.

**(Choice B)** Diffuse esophageal spasm is a motility disorder characterized by episodic, painful, non-propulsive esophageal smooth muscle contraction. Biliary colic is similar to esophageal spasm in that gallbladder contraction against an obstructed cystic duct results in postprandial epigastric pain.





gallbladder contraction against an obstructed cystic duct results in postprandial epigastric pain.

**(Choice C)** Peptic ulcer disease is characterized by gastrointestinal erosions/ulcerations and is typically due to *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug use. This patient's pain did not respond to antacids and his upper endoscopy is normal, so he is unlikely to have a condition associated with peptic ulcers.

**(Choice D)** Pulmonary embolism is often due to an embolic blood clot lodging in the branches of the pulmonary artery, resulting in acute pulmonary ischemia/infarction. A similar pathogenesis accounts for acute mesenteric ischemia, which can occur with superior mesenteric artery embolism. This condition is more likely to cause sudden, severe abdominal pain rather than recurrent postprandial abdominal pain with food aversion.

### Educational objective:

Chronic mesenteric ischemia is characterized by atherosclerosis of the mesenteric arteries, resulting in diminished blood flow to the intestine after meals. This causes postprandial epigastric pain (intestinal angina) with associated food aversion/weight loss. Its pathogenesis is similar to angina pectoris.

### References

- [Chronic mesenteric ischemia: diagnosis and management.](#)







A 4-week-old boy is hospitalized with persistent vomiting, fussiness, and feeding intolerance. The emesis was initially clear but became bilious in the last few hours. The infant had been breastfeeding exclusively. His temperature is 37.2 C (99.0 F). Blood pressure and pulse are normal. Physical examination shows a normal abdomen with no rebound or guarding. An upper gastrointestinal series is obtained urgently to evaluate for malrotation and volvulus and shows normal rotation but constriction of the duodenum. An abdominal CT scan reveals pancreatic tissue encircling the duodenum. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Aberrant differentiation of the midgut structures
- ☐ B. Abnormal migration of the ventral pancreatic bud
- ☐ C. Ectopic rests not connected to the pancreas
- ☐ D. Failure of apoptosis in the dorsal pancreatic bud
- ☐ E. Failure of the ventral and dorsal pancreatic bud to fuse

**Submit**



A 4-week-old boy is hospitalized with persistent vomiting, fussiness, and feeding intolerance. The emesis was initially clear but became bilious in the last few hours. The infant had been breastfeeding exclusively. His temperature is 37.2 C (99.0 F). Blood pressure and pulse are normal. Physical examination shows a normal abdomen with no rebound or guarding. An upper gastrointestinal series is obtained urgently to evaluate for malrotation and volvulus and shows normal rotation but constriction of the duodenum. An abdominal CT scan reveals pancreatic tissue encircling the duodenum. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Aberrant differentiation of the midgut structures (0%)
- ☒ B. Abnormal migration of the ventral pancreatic bud (74%)
- ☐ C. Ectopic rests not connected to the pancreas (1%)
- ☐ D. Failure of apoptosis in the dorsal pancreatic bud (6%)
- ☐ E. Failure of the ventral and dorsal pancreatic bud to fuse (16%)





Item 19 of 40

Question Id: 438



Mark



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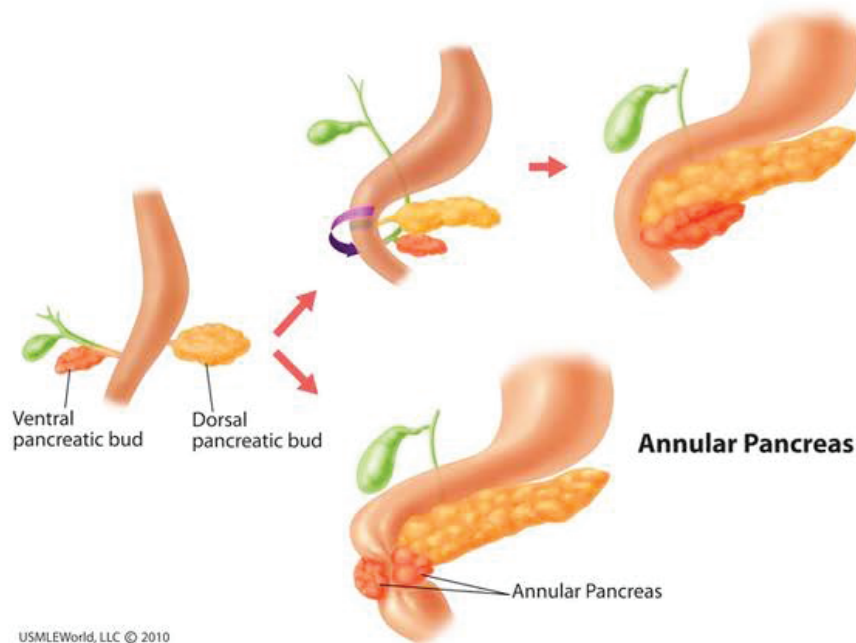
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### Exhibit Display

#### Normal Pancreas development



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This patient has acute pancreatitis and radiographic evidence of **annular pancreas**, which results from abnormal migration of the ventral pancreatic bud. This bud is a **foregut** derivative that appears by the fifth week of gestation and **rotates behind** the duodenum during the seventh week of fetal development. The ventral bud moves toward the midline, where it fuses with the dorsal pancreatic bud during the eighth week. The ventral pancreatic bud gives rise to the **uncinate process** portion of the head and the **main pancreatic duct** (of Wirsung). The pancreatic tail, body, and the remainder of head derive from the dorsal bud.

Abnormal migration of the ventral pancreatic bud can be caused by adherence to either the dorsal bud or duodenum before the rotation begins. This abnormal migration leads to **annular pancreas**, a rare congenital anomaly in which pancreatic tissue completely surrounds the second part of the duodenum. Annular pancreas can compress the duodenal lumen (causing **obstruction**) or result in obstructed pancreatic drainage (acute or chronic **pancreatitis**). However, the majority of patients with annular pancreas are **asymptomatic**.

**(Choice A)** The pancreas is not derived from the midgut. Both ventral and dorsal pancreatic buds form from the duodenal portion of the foregut.

**(Choice C)** Ectopic rests, or fragments of embryonic tissue that persist beyond the fetal period, can be





**(Choice A)** The pancreas is not derived from the midgut. Both ventral and dorsal pancreatic buds form from the duodenal portion of the foregut.

**(Choice C)** Ectopic rests, or fragments of embryonic tissue that persist beyond the fetal period, can be found throughout the gastrointestinal tract. However, the pancreatic tissue in annular pancreas is contiguous with the rest of the pancreas by definition.

**(Choice D)** Neither the dorsal nor ventral pancreatic bud undergoes apoptosis in normal development.

**(Choice E)** Incomplete fusion of the ventral and dorsal pancreatic buds (pancreas divisum) is usually asymptomatic and much more common than annular pancreas. Pancreas divisum does not cause obstruction as the duodenum is not completely encircled but may predispose to the development of acute or chronic pancreatitis.

### Educational objective:

Annular pancreas, or pancreatic tissue encircling the descending duodenum, is caused by failure of the ventral pancreatic bud to properly migrate and fuse with the dorsal bud during the seventh and eighth week of fetal development. Annular pancreas is usually asymptomatic but may present with duodenal obstruction or pancreatitis.

### References





A 44-year-old man with a long-standing history of heartburn comes to the office due to worsening substernal burning, particularly at night. The discomfort has been less responsive than usual to over-the-counter antacids. The patient also now has significant substernal pain after swallowing food. However, swallowing does not result in coughing, choking, or a sensation of food getting stuck. He has no other chronic medical conditions. Recent HIV testing was negative. The patient takes no other medications. He drinks 2 or 3 beers each evening and smokes a pack of cigarettes daily. BMI is 34 kg/m<sup>2</sup>. Vital signs are within normal limits. Physical examination reveals no abnormalities. The recent worsening of this patient's symptoms is most likely related to which of the following?

- ☐ A. Columnar metaplasia
- ☐ B. Herpes simplex infection
- ☐ C. Malignancy
- ☐ D. Stricture
- ☐ E. Ulceration







substernal burning, particularly at night. The discomfort has been **less responsive** than usual to over-the-counter antacids. The patient also now has significant substernal pain after swallowing food. However, swallowing does not result in coughing, choking, or a sensation of food getting stuck. He has no other chronic medical conditions. Recent HIV testing was negative. The patient takes no other medications. He drinks 2 or 3 beers each evening and smokes a pack of cigarettes daily. **BMI** is 34 kg/m<sup>2</sup>. Vital signs are within normal limits. Physical examination reveals no abnormalities. The recent worsening of this patient's symptoms is most likely related to which of the following?

- ☐ A. Columnar metaplasia (33%)
- ☐ B. Herpes simplex infection (1%)
- ☐ C. Malignancy (11%)
- ☐ D. Stricture (5%)
- ✓ ☒ E. Ulceration (47%)

Correct

47%



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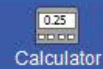
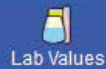
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## Gastroesophageal reflux disease

### Pathophysiology

- Decreased tone or excessive transient relaxation of LES
- Anatomic disruption to gastroesophageal junction (eg, hiatal hernia)
- ↑ Risk with obesity, pregnancy, smoking, alcohol intake

### Manifestations

- Regurgitation of acidic material in mouth
- **Heartburn**
- Odynophagia (often indicates reflux esophagitis)
- Extraesophageal symptoms (eg, cough, laryngitis, wheezing)

### Complications

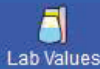
- Erosive esophagitis
- Strictures
- Barrett esophagus → adenocarcinoma

### Initial treatment

- Lifestyle (eg, weight loss) & dietary changes
- H2R blocker or proton pump inhibitor

**H2R** = histamine 2 receptor; **LES** = lower esophageal sphincter.





**Gastroesophageal reflux disease** (GERD) is caused by the retrograde flow of acidic stomach contents through the lower esophageal sphincter into the esophagus. Common symptoms include burning pain in the retrosternal area (**heartburn**) and **acid regurgitation** into the back of the mouth. GERD usually does not cause esophageal mucosal injury, but frequent exposure to highly acidic secretions can overwhelm esophageal mucosal defense mechanisms and result in epithelial damage and **complications**, such as:

- **Erosive esophagitis** with esophageal **ulcers** - often marked by a worsening of baseline GERD symptoms and the development of **odynophagia** (painful swallowing).
- Barrett esophagus - metaplastic columnar epithelium replaces the normal stratified squamous epithelium in the distal esophagus. Most cases are asymptomatic with no change in baseline GERD manifestations. However, Barrett esophagus is a premalignant condition for esophageal adenocarcinoma, which typically presents with dysphagia and weight loss (**Choices A and C**).
- Esophageal stricture - typically develops in the setting of a healing esophageal ulcer when collagen fibers contract and cause narrowing of the esophageal lumen. Patients usually present with dysphagia and a sensation of food getting stuck in the esophagus (**Choice D**).

(**Choice B**) Infectious esophagitis can be caused by a number of agents, including cytomegalovirus,







- Esophageal stricture - typically develops in the setting of a healing esophageal ulcer when collagen fibers contract and cause narrowing of the esophageal lumen. Patients usually present with dysphagia and a sensation of food getting stuck in the esophagus **(Choice D)**.

**(Choice B)** Infectious esophagitis can be caused by a number of agents, including cytomegalovirus, Candida, and herpes simplex virus. However, it occurs most commonly in immunosuppressed patients (eg, AIDS, prolonged steroids). This patient has no evidence of an immunocompromised state (eg, recent HIV testing was negative) and has long-standing GERD, making erosive esophagitis more likely.

### Educational objective:

New-onset odynophagia in the setting of chronic gastroesophageal reflux disease should raise suspicion for erosive esophagitis with esophageal ulcers. Diagnosis is made by upper endoscopy.

### References

- [Pathophysiology of gastro-oesophageal reflux disease.](#)

Pathophysiology

Gastrointestinal &amp; Nutrition

Gastroesophageal reflux disease

Subject

System

Topic

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A 65-year-old man with a history of hypertension, type 2 diabetes mellitus, and tobacco smoking comes to the office reporting mild back pain. Abdominal examination reveals a bruit, but no pulsatile mass is palpated. Femoral and pedal pulses are symmetric. The patient is sent for ultrasound and is found to have a large infrarenal abdominal aortic aneurysm. Open aneurysm repair is performed. During the procedure, the inferior mesenteric artery is ligated, the diseased portion of the aorta is dissected, and a graft is placed from below the renal arteries to the bifurcation of the aorta. Collateral circulation from which of the following vessels is most likely responsible for preventing ischemia of the descending colon?

- ☐ A. Celiac trunk
- ☐ B. External iliac artery
- ☐ C. Inferior vena cava
- ☐ D. Internal iliac artery
- ☐ E. Portal vein
- ☐ F. Renal artery
- ☐ G. Superior mesenteric artery





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Previous

Next

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Lab Values

Notes

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the office reporting mild back pain. Abdominal examination reveals a bruit, but no pulsatile mass is palpated. Femoral and pedal pulses are symmetric. The patient is sent for ultrasound and is found to have a large infrarenal abdominal aortic aneurysm. Open aneurysm repair is performed. During the procedure, the inferior mesenteric artery is ligated, the diseased portion of the aorta is dissected, and a graft is placed from below the renal arteries to the bifurcation of the aorta. Collateral circulation from which of the following vessels is most likely responsible for preventing ischemia of the descending colon?

- ☐ A. Celiac trunk (2%)
- ☐ B. External iliac artery (6%)
- ☐ C. Inferior vena cava (0%)
- ☐ D. Internal iliac artery (20%)
- ☐ E. Portal vein (1%)
- ☐ F. Renal artery (2%)
- ☒ G. Superior mesenteric artery (65%)

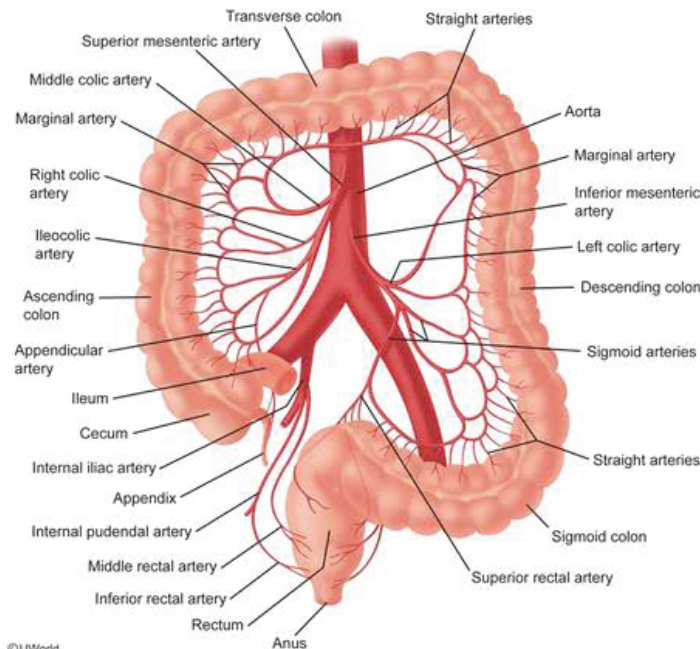






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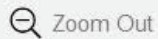
## Arteries of the large intestine



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The gastrointestinal tract receives its blood supply from 3 main arteries:

- Celiac trunk
- **Superior mesenteric artery (SMA)**
- **Inferior mesenteric artery (IMA)**

The celiac trunk supplies the stomach, part of the duodenum, gallbladder, liver, spleen, and pancreas (**Choice A**). The SMA and IMA are the 2 main vessels supplying the small and large intestines and are connected by a pair of anastomoses: the **marginal artery** of Drummond, which is the principal **anastomosis**, and the inconsistently present arc of Riolan (mesenteric meandering artery). These anastomoses protect the intestines from ischemia and, due to the marginal artery, the IMA is not always reconnected during aortic aneurysm repair.

(**Choice B**) The **external iliac artery** supplies the inferior epigastric artery and the deep circumflex iliac artery before becoming the femoral artery. Although the inferior epigastric artery anastomoses with the superior epigastric artery, these provide blood supply to the abdominal wall, not the intestines.

(**Choices C and E**) The inferior vena cava (IVC) has little role in the direct drainage of the intestines except from the rectum, which partially drains via the middle and inferior rectal veins into the internal iliac





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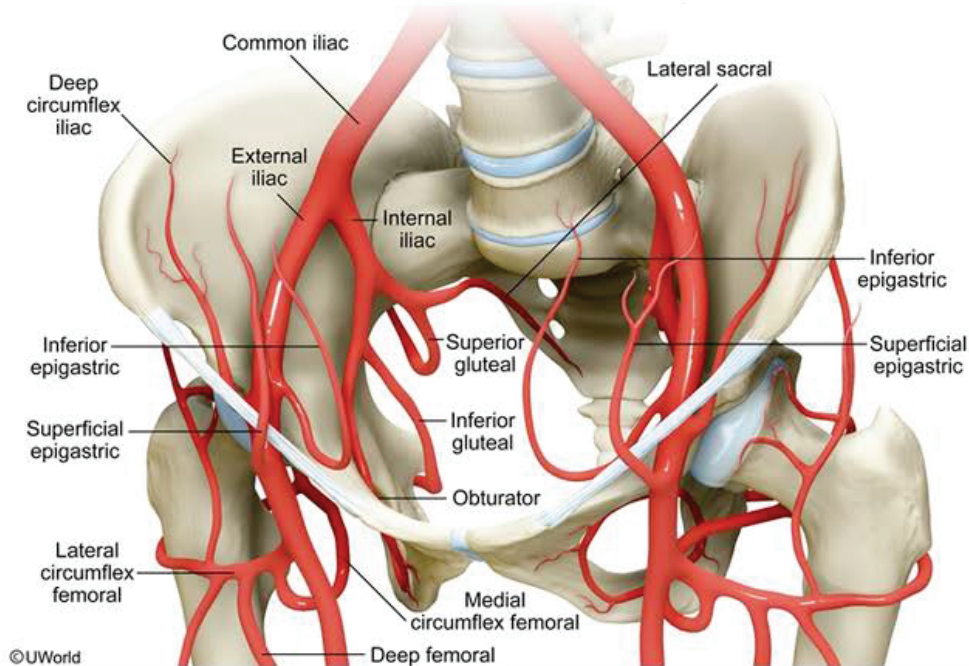
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## Exhibit Display

## Branches of common iliac artery



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superior epigastric artery, these provide blood supply to the abdominal wall, not the intestines.

**(Choices C and E)** The inferior vena cava (IVC) has little role in the direct drainage of the intestines except from the rectum, which partially drains via the middle and inferior rectal veins into the internal iliac veins. The remainder of the **venous drainage** occurs via the superior and inferior mesenteric veins, which drain into the portal vein. After perfusing the liver, the portal vein drains into the IVC via the hepatic veins.

**(Choice D)** The internal iliac artery supplies part of the rectum via the middle rectal artery. An anastomosis exists between the superior and middle rectal arteries, which can help prevent rectal ischemia after IMA occlusion. However, the SMA is more likely to prevent ischemia in the descending colon due to its proximity and the extensive collateral arcades between the SMA and IMA.

**(Choice F)** Although the renal arteries arise from the abdominal aorta just inferior to the SMA, they do not provide collateral circulation to the intestines.

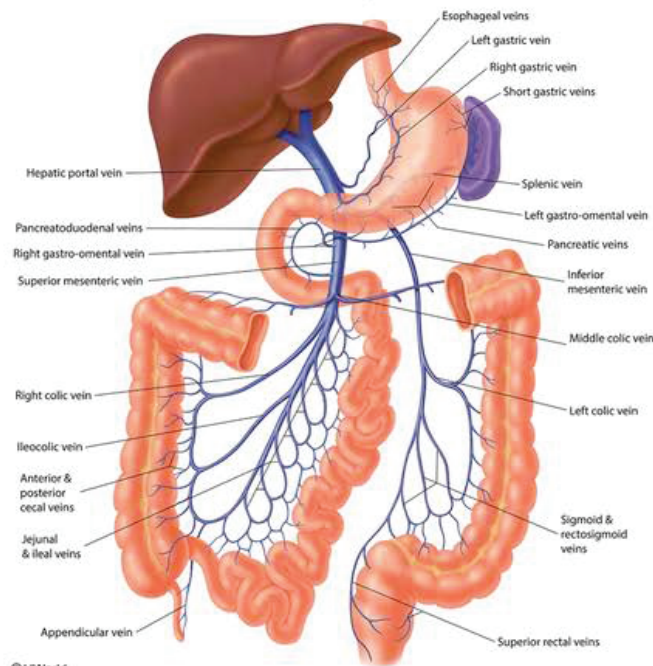
### **Educational objective:**

The superior mesenteric artery and inferior mesenteric artery are the 2 main vessels supplying the small and large intestines. They are connected by a pair of anastomoses: the marginal artery of Drummond, which is the principal anastomosis, and the inconsistently present arc of Riolan (mesenteric meandering artery).

superior epigastric artery, these provide blood supply to the abdominal wall, not the intestines.

## Exhibit Display

## Portal venous system



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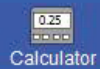
A 62-year-old man is hospitalized with severe abdominal pain and diarrhea after a recent urinary tract infection. Six months ago, the patient had an episode of *Clostridium difficile* colitis after being treated for pneumonia. Medical history is also significant for diverticulitis and upper gastrointestinal tract bleeding. The patient is allergic to penicillin. An appropriate workup confirms *C difficile* colitis. The patient is placed on an oral macrocyclic antibiotic that inhibits the sigma subunit of RNA polymerase. Which of the following agents was most likely administered to this patient?

- ☐ A. Doxycycline
- ☐ B. Fidaxomicin
- ☐ C. Metronidazole
- ☐ D. Neomycin
- ☐ E. Vancomycin

Submit







A 62-year-old man is hospitalized with severe abdominal pain and diarrhea after a recent urinary tract infection. Six months ago, the patient had an episode of *Clostridium difficile* colitis after being treated for pneumonia. Medical history is also significant for diverticulitis and upper gastrointestinal tract bleeding. The patient is allergic to penicillin. An appropriate workup confirms *C difficile* colitis. The patient is placed on an oral macrocyclic antibiotic that inhibits the sigma subunit of RNA polymerase. Which of the following agents was most likely administered to this patient?

- ☐ A. Doxycycline (10%)
- ✓ ☒ B. Fidaxomicin (33%)
- ☐ C. Metronidazole (35%)
- ☐ D. Neomycin (8%)
- ☐ E. Vancomycin (11%)

Correct

33%  
Answered correctly

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Treatment options for ***Clostridium difficile*** infection (CDI) typically include oral vancomycin or fidaxomicin. **Fidaxomicin** is a macrocyclic antibiotic (related to macrolides) that **inhibits** the sigma subunit of **RNA polymerase**, leading to protein synthesis impairment and cell death (**bactericidal** activity against *C difficile*). It is administered orally and has minimal systemic absorption, resulting in high fecal concentrations. It also has a narrow spectrum of activity with a lesser effect on normal colonic flora than vancomycin.

**(Choice A)** Doxycycline binds to the 30S ribosomal subunit and is effective in clostridial skin infections (eg, *C perfringens*, *C septicum*), but it is not effective for treatment of CDI.

**(Choice C)** Metronidazole interacts with DNA in anaerobic organisms, disrupting DNA structure and causing strand breakage. Intravenous metronidazole can be a useful adjunct in patients with severe CDI (eg, megacolon, ileus, hypotension), since these patients often have delayed passage of oral antibiotics.

**(Choice D)** Neomycin is a bactericidal aminoglycoside that inhibits the 30S ribosomal subunit. It can be used to treat hepatic encephalopathy or diarrhea due to *Escherichia coli* and as surgical prophylaxis for gastrointestinal procedures. However, it is not effective against *C difficile*.

**(Choice E)** Oral vancomycin has minimal systemic absorption and is often used to treat initial or recurrent CDI. It inhibits cell wall synthesis and is bacteriostatic against *C difficile* at the concentrations typically





**(Choice C)** Metronidazole interacts with DNA in anaerobic organisms, disrupting DNA structure and causing strand breakage. Intravenous metronidazole can be a useful adjunct in patients with severe CDI (eg, megacolon, ileus, hypotension), since these patients often have delayed passage of oral antibiotics.

**(Choice D)** Neomycin is a bactericidal aminoglycoside that inhibits the 30S ribosomal subunit. It can be used to treat hepatic encephalopathy or diarrhea due to *Escherichia coli* and as surgical prophylaxis for gastrointestinal procedures. However, it is not effective against *C difficile*.

**(Choice E)** Oral vancomycin has minimal systemic absorption and is often used to treat initial or recurrent CDI. It inhibits cell wall synthesis and is bacteriostatic against *C difficile* at the concentrations typically used for CDI treatment.

### Educational objective:

*Clostridium difficile* infection can be treated with oral vancomycin or fidaxomicin. Fidaxomicin is a macrocyclic antibiotic that inhibits RNA polymerase. It is bactericidal against *C difficile*.

### References

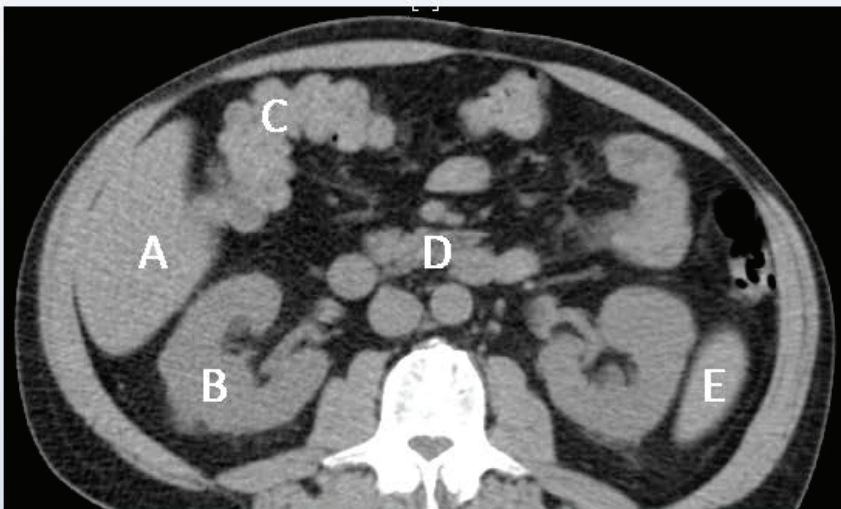
- Fidaxomicin: a novel macrocyclic antibiotic approved for treatment of *Clostridium difficile* infection.
- Bactericidal activity of telavancin, vancomycin and metronidazole against *Clostridium difficile*.



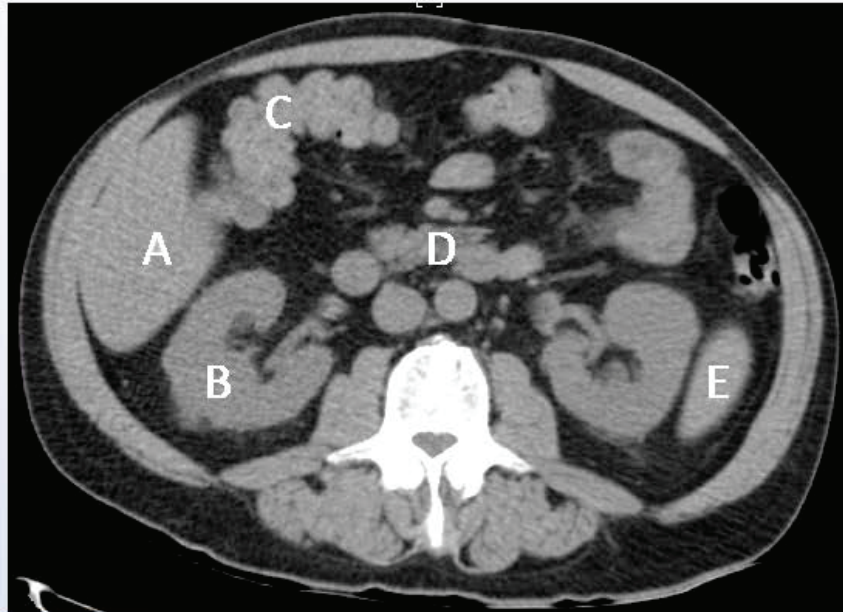




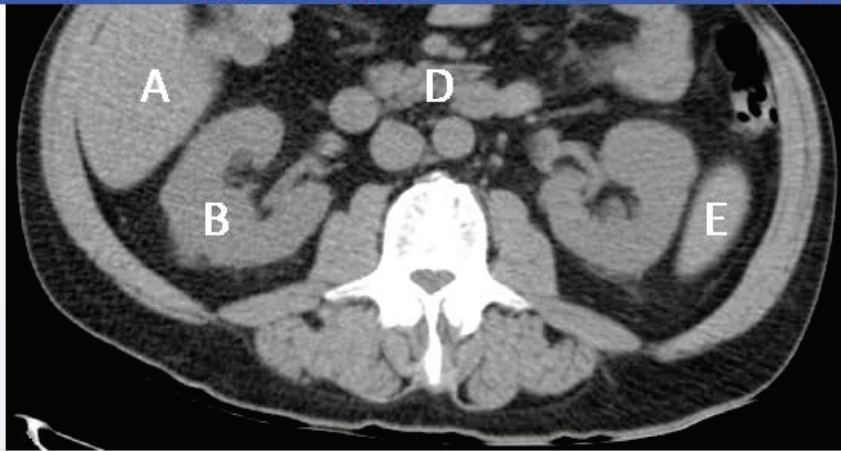
A 35-year-old man comes to the emergency department due to persistent abdominal pain. Yesterday, during a soccer game, he suffered a full-speed collision with another player. He had diffuse abdominal pain at the time but did not seek care until this morning, when the pain seemed to worsen. As part of the patient's evaluation, a CT scan of the abdomen is obtained and shown in the image below. It is determined that his injury involves an organ that is supplied mainly by an artery of the foregut even though the organ itself is not a foregut derivative. Which of the following organs is most likely to be injured in this patient?



patient's evaluation, a CT scan of the abdomen is obtained and shown in the image below. It is determined that his injury involves an organ that is supplied mainly by an artery of the foregut even though the organ itself is not a foregut derivative. Which of the following organs is most likely to be injured in this patient?



☐ A.A



- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E





Mark



Previous



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Settings



- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☒ E.E



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Feedback



Suspend



End Block



- ☐ A.A (9%)
- ☐ B.B (3%)
- ☐ C.C (5%)
- ☐ D.D (11%)
- ✓ ☒ E.E (69%)

Correct

69%

48 secs

01/09/2021

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Feedback



Suspend



End Block



The most common intra-abdominal organ injured during **blunt trauma** is the **spleen**. CT scans and MRI are conventionally presented so that the patient's left is on the reader's right (imagine that the patient is supine with the feet directed toward the viewer). This is a relatively caudal (lower) abdominal image that includes the kidneys; therefore, only the tail of the spleen is visible.

The spleen is an intraperitoneal organ derived from the **mesoderm** of the dorsal mesentery. However, the spleen is unique in that its blood supply derives from a **foregut derivative** (the splenic artery off of the **celiac trunk**). Venous return from the spleen courses through the **splenic vein** to return to the portal circulation rather than the systemic circulation.

**(Choice A)** The liver is an endoderm-derived structure of the foregut and receives its arterial blood from the proper hepatic artery (via the celiac trunk). The liver also receives venous blood from the gut via the portal vein.

**(Choice B)** Like the spleen, the kidneys are derived from the mesoderm. However, the kidneys are retroperitoneal and supplied by the renal arteries (from the abdominal aorta) and drained by the renal veins (to the inferior vena cava).

**(Choice C)** The first two-thirds of the transverse colon is derived from the midgut and supplied by the superior mesenteric artery. The last one-third of the transverse colon arises from the hindgut and is







**(Choice B)** Like the spleen, the kidneys are derived from the mesoderm. However, the kidneys are retroperitoneal and supplied by the renal arteries (from the abdominal aorta) and drained by the renal veins (to the inferior vena cava).

**(Choice C)** The first two-thirds of the transverse colon is derived from the midgut and supplied by the superior mesenteric artery. The last one-third of the transverse colon arises from the hindgut and is supplied by branches of the inferior mesenteric artery. These 2 vessels anastomose via the marginal artery.

**(Choice D)** The pancreas is an endoderm-derived structure of the foregut that receives blood primarily from the superior and inferior pancreaticoduodenal arteries.

### Educational objective:

The spleen is of mesodermal origin (the dorsal mesentery). Although it is supplied by the splenic artery (a branch of the major foregut vessel, the celiac trunk), it is not a foregut derivative.

### References

- [Embryonic origins of spleen asymmetry.](#)

Embryology

Gastrointestinal &amp; Nutrition

Spleen rupture

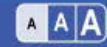




A 65-year-old man is referred to a gastroenterology clinic by his primary care provider after he develops symptoms suspicious for colorectal cancer. The patient has a history of obesity, diabetes mellitus, and chronic obstructive pulmonary disease. He often eats steaks and hamburgers but avoids vegetables as "they have no flavor." The patient has smoked a pack of cigarettes daily for the past 40 years and occasionally consumes alcohol. He undergoes a colonoscopy and is found to have a mass lesion in the ascending colon. The mass is biopsied, and the histopathologic findings are consistent with colon adenocarcinoma. This patient most likely initially presented with which of the following clinical symptoms?

- ☐ A. Abdominal pain, distension, and nausea
- ☐ B. Constipation alternating with diarrhea
- ☐ C. Recurrent grossly bloody stool and low-grade fever
- ☐ D. Tenesmus and small-caliber stool
- ☐ E. Weight loss and progressive fatigue

**Submit**



A 65-year-old man is referred to a gastroenterology clinic by his primary care provider after he develops symptoms suspicious for colorectal cancer. The patient has a history of obesity, diabetes mellitus, and chronic obstructive pulmonary disease. He often eats steaks and hamburgers but avoids vegetables as "they have no flavor." The patient has smoked a pack of cigarettes daily for the past 40 years and occasionally consumes alcohol. He undergoes a colonoscopy and is found to have a mass lesion in the ascending colon. The mass is biopsied, and the histopathologic findings are consistent with colon adenocarcinoma. This patient most likely initially presented with which of the following clinical symptoms?

- ☐ A. Abdominal pain, distension, and nausea (6%)
- ☐ B. Constipation alternating with diarrhea (8%)
- ☐ C. Recurrent grossly bloody stool and low-grade fever (19%)
- ☐ D. Tenesmus and small-caliber stool (7%)
- ☒ E. Weight loss and progressive fatigue (58%)







The location of colon adenocarcinoma can influence its clinical manifestations. **Right-sided colon cancers** usually grow as exophytic masses. Patients generally do not develop intestinal obstruction because the ascending colon has a larger caliber lumen than the descending colon and stool in the proximal colon is more liquid. Right-sided colon cancers typically present with features of **iron deficiency anemia** (eg, fatigue, pallor) due to occult blood loss. Nonspecific symptoms such as anorexia, malaise, and unintentional weight loss may also occur.

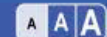
Environmental and lifestyle factors that may have increased this patient's risk of colon cancer include obesity, cigarette smoking, consumption of red/processed meat, and low dietary intake of vegetables.

**(Choice A)** Left-sided colon cancers tend to infiltrate the intestinal wall and encircle the lumen, causing a change in bowel habits (eg, constipation) and symptoms of intestinal obstruction (eg, abdominal pain, distension, nausea/vomiting).

**(Choice B)** Constipation that alternates with diarrhea is characteristic of irritable bowel syndrome.

**(Choice C)** Recurrent grossly bloody stool associated with abdominal discomfort and low-grade fever is characteristic of ulcerative colitis, which is a risk factor for colon cancer. Rectosigmoid cancer often causes hematochezia, but fever is uncommon.





change in bowel habits (eg, constipation) and symptoms of intestinal obstruction (eg, abdominal pain, distension, nausea/vomiting).

**(Choice B)** Constipation that alternates with diarrhea is characteristic of irritable bowel syndrome.

**(Choice C)** Recurrent grossly bloody stool associated with abdominal discomfort and low-grade fever is characteristic of ulcerative colitis, which is a risk factor for colon cancer. Rectosigmoid cancer often causes hematochezia, but fever is uncommon.

**(Choice D)** Tenesmus (ineffectual/painful straining on defecation) and small-caliber stool are characteristic of rectal adenocarcinoma.

### Educational objective:

Right-sided colon cancers usually grow as exophytic masses and present with occult bleeding and symptoms of iron deficiency anemia. Left-sided colon cancers tend to infiltrate the intestinal wall and encircle the lumen, causing constipation and symptoms of intestinal obstruction. Rectosigmoid involvement often causes hematochezia.

### References

- [Left and right sided large bowel cancer.](#)





A 74-year-old man comes to the office due to chronic constipation. Bowel movements occur once every 3 days and are hard and pellet-like. The patient frequently strains when he tries to defecate and never feels completely evacuated. The constipation is occasionally so severe that he uses his fingers to remove stool from the anorectal vault. Medical history is significant for Parkinson disease, for which he takes carbidopa-levodopa. Vital signs are unremarkable. A resting tremor is present on physical examination. The abdomen is distended but nontender to palpation. This patient's condition is most likely due to inadequate relaxation of which of the following muscles during defecation?

- ☐ A. Bulbospongiosus
- ☐ B. Obturator
- ☐ C. Piriformis
- ☐ D. Puborectalis
- ☐ E. Rectus abdominis

**Submit**





A 74-year-old man comes to the office due to **chronic constipation**. Bowel movements occur once every 3 days and are hard and **pellet-like**. The patient frequently strains when he tries to defecate and never feels completely evacuated. The constipation is occasionally so severe that he uses his fingers to remove stool from the anorectal vault. Medical history is significant for Parkinson disease, for which he takes carbidopa-levodopa. Vital signs are unremarkable. A resting tremor is present on physical examination. The abdomen is distended but nontender to palpation. This patient's condition is most likely due to inadequate relaxation of which of the following muscles during defecation?

- ☐ A. Bulbospongiosus (6%)
- ☐ B. Obturator (2%)
- ☐ C. Piriformis (5%)
- ☒ D. Puborectalis (80%)
- ☐ E. Rectus abdominis (5%)





Stool continence is largely maintained by tonic contraction of the internal and external anal sphincter and the puborectalis muscle, which forms a muscular sling around the rectum and squeezes it into a narrow angle to prevent stool leakage. **Defecation** requires the coordinated relaxation of these muscles, which occurs as follows:

1. Distension of the rectal vault activates mechanoreceptors that cause involuntary relaxation of the internal anal sphincter (rectosphincteric reflex) and an urge to defecate.
2. The puborectalis muscle and external anal sphincter are under voluntary control; when defecation is desired, the muscles relax and the rectum contracts, expelling feces.
3. The abdominal muscles contract to increase the pressure gradient of the rectum and aid in the rapid expulsion of feces.

If the internal or external anal sphincter or, more commonly, the **puborectalis muscle fails to relax**, stool remains in the rectal vault despite attempts to initiate bowel movements (**dyssynergia**), resulting in chronic **constipation**. Patients often strain for a long time only to pass small amounts of stool, and manual disimpaction may be required. Dyssynergic defecation is usually considered a functional disorder and occurs more commonly in the elderly; however, it can occur with certain neurologic disorders (eg,





occurs more commonly in the elderly; however, it can occur with certain neurologic disorders (eg, Parkinson disease, multiple sclerosis) or trauma.

**(Choice A)** The bulbospongiosus is a superficial perineal muscle that enables penile erection and ejaculation in men and facilitates both vaginal canal closure and orgasm in women. Its dysfunction would lead to sexual impairment but not defecatory dysfunction.

**(Choices B and C)** The obturator internus and externus and the piriformis contribute to lateral hip rotation. Dysfunction in these muscles would result in motor impairment and gait abnormalities, not defecatory dysfunction.

**(Choice E)** The rectus abdominis consists of 2 large, paired muscles that run vertically along the anterior abdominal wall. Contraction of abdominal muscles increases the pressure gradient of the rectum and aids in the rapid expulsion of feces; failure of this muscle to relax would not result in constipation.

### Educational objective:

Dyssynergic defecation occurs when the puborectalis muscle or the internal or external anal sphincter fails to relax during defecation, leading to chronic constipation. Dyssynergic defecation is usually considered a functional disorder and occurs more commonly in the elderly but may also occur with certain neurologic disorders (eg, Parkinson disease, multiple sclerosis) or trauma.







A 62-year-old woman comes to the office due to a change in bowel habits. For 2 months, she has had bowel movements once every 5 or 6 days. The patient describes her stools as hard and lumpy and of small volume; defecation is uncomfortable. She has no trouble passing gas and has no other symptoms, including no nausea, vomiting, or weight changes. The patient was admitted to the hospital 3 months ago for acute diverticulitis, and her hospital course was complicated by new-onset atrial fibrillation. Colonoscopy a month after hospitalization revealed sigmoid diverticulosis but no masses or polyps. The patient takes fiber supplements, diltiazem, and apixaban. She does not use tobacco or alcohol. Vital signs are within normal limits. Cardiac auscultation reveals an irregular heart rhythm but no murmurs. Abdominal examination is significant for mild distension. Which of the following best explains this patient's symptoms?

- ☐ A. Alterations in colonic microbiome
- ☐ B. Gastrocolic reflex impairment
- ☐ C. Inappropriate contraction of pelvic floor muscles
- ☐ D. Medication adverse effects
- ☐ E. Posterior vaginal wall prolapse





including no nausea, vomiting, or weight changes. The patient was admitted to the hospital 5 months ago

for acute diverticulitis, and her hospital course was complicated by new-onset atrial fibrillation.

Colonoscopy a month after hospitalization revealed sigmoid diverticulosis but no masses or polyps. The patient takes fiber supplements, diltiazem, and apixaban. She does not use tobacco or alcohol. Vital signs are within normal limits. Cardiac auscultation reveals an irregular heart rhythm but no murmurs.

Abdominal examination is significant for mild distension. Which of the following best explains this patient's symptoms?

- ☐ A. Alterations in colonic microbiome
- ☐ B. Gastrocolic reflex impairment
- ☐ C. Inappropriate contraction of pelvic floor muscles
- ☐ D. Medication adverse effects
- ☐ E. Posterior vaginal wall prolapse
- ☐ F. Sigmoid volvulus

Submit

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Feedback



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End Block



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for acute diverticulitis, and her hospital course was complicated by new-onset atrial fibrillation.

Colonoscopy a month after hospitalization revealed sigmoid diverticulosis but no masses or polyps. The patient takes fiber supplements, diltiazem, and apixaban. She does not use tobacco or alcohol. Vital signs are within normal limits. Cardiac auscultation reveals an irregular heart rhythm but no murmurs.

Abdominal examination is significant for mild distension. Which of the following best explains this patient's symptoms?

- ☐ A. Alterations in colonic microbiome (6%)
- ☐ B. Gastrocolic reflex impairment (11%)
- ☐ C. Inappropriate contraction of pelvic floor muscles (2%)
- ☒ D. Medication adverse effects (66%)
- ☐ E. Posterior vaginal wall prolapse (3%)
- ☐ F. Sigmoid volvulus (9%)





### Common medications associated with constipation

<b>Opioids</b>	<ul style="list-style-type: none"><li>• Centrally acting (eg, oxycodone, morphine)</li><li>• Peripherally acting (eg, loperamide)</li></ul>
<b>Anticholinergic agents</b>	<ul style="list-style-type: none"><li>• Antihistamines (eg, diphenhydramine)</li><li>• Tricyclic antidepressants (eg, amitriptyline)</li><li>• Antispasmodics (eg, dicyclomine)</li><li>• 1st-generation antipsychotics (eg, haloperidol)</li></ul>
<b>Cation-containing agents</b>	<ul style="list-style-type: none"><li>• Iron tablets</li><li>• Aluminum (eg, antacids)</li></ul>
<b>Non-dihydropyridine calcium channel blockers</b>	<ul style="list-style-type: none"><li>• Diltiazem, verapamil</li></ul>
<b>5HT<sub>3</sub> antagonists</b>	<ul style="list-style-type: none"><li>• Ondansetron, granisetron</li></ul>

5-HT<sub>3</sub> = 5-hydroxytryptamine type 3.



**Constipation** is an exceedingly common gastrointestinal condition with a wide variety of underlying etiologies (eg, autonomic neuropathy, hypothyroidism, electrolyte abnormalities). In this patient who developed constipation after new-onset atrial fibrillation, the most likely etiology is a **drug effect** related to diltiazem.

Diltiazem and verapamil are **non-dihydropyridine calcium channel blockers** that decrease conduction velocity in the sinoatrial and atrioventricular nodes and are often used in the management of atrial fibrillation. Constipation, a common adverse effect, occurs due to inhibition of the colonic migrating motor complex, resulting in **slowed contractions of colonic smooth muscle**. This is not typically seen with dihydropyridine calcium channel blockers (eg, amlodipine, nifedipine).

Other common medications that cause constipation include opiates, serotonin 5-HT<sub>3</sub> antagonists (eg, ondansetron), iron tablets, aluminum-containing agents (eg, antacids), and medications with anticholinergic properties (eg, diphenhydramine, tricyclic antidepressants, first-generation antipsychotics).

**(Choice A)** Alterations in the colonic microbiome are common after antibiotic therapy but typically cause diarrhea (eg, *Clostridioides* [formerly *Clostridium*] *difficile* colitis), not constipation.

**(Choice B)** The gastrocolic reflex is a neurogenic reflex triggered by gastric distension from food, leading





properties (eg, diphenhydramine, tricyclic antidepressants, first-generation antipsychotics).

**(Choice A)** Alterations in the colonic microbiome are common after antibiotic therapy but typically cause diarrhea (eg, *Clostridioides* [formerly *Clostridium*] *difficile* colitis), not constipation.

**(Choice B)** The gastrocolic reflex is a neurogenic reflex triggered by gastric distension from food, leading to colonic contractions; impairment of the reflex can cause constipation. However, this typically occurs in patients with diabetic neuropathy and gastroparesis.

**(Choice C)** Inappropriate contraction of pelvic floor muscles occurs with dyssnergic defecation, preventing the expulsion of stool from the rectum. Dyssnergic defecation is more common in the elderly and often associated with neurologic disorders (eg, Parkinson disease) or trauma. The development of symptoms after this patient started diltiazem is more consistent with medication-induced constipation.

**(Choice E)** A rectocele, which occurs when the rectum prolapses into the posterior vaginal wall, usually develops in elderly, multiparous women. Although constipation is common, patients usually describe pelvic pressure and the need to manually push on the vagina or rectum to defecate.

**(Choice F)** Sigmoid volvulus typically presents with progressive abdominal pain, nausea, and constipation and eventually results in bowel obstruction (eg, failure to pass gas, obstipation, possible perforation).

Symptoms occur over the course of days, not months.





**(Choice C)** Inappropriate contraction of pelvic floor muscles occurs with dyssnergic defecation, preventing the expulsion of stool from the rectum. Dyssnergic defecation is more common in the elderly and often associated with neurologic disorders (eg, Parkinson disease) or trauma. The development of symptoms after this patient started diltiazem is more consistent with medication-induced constipation.

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**(Choice F)** Sigmoid volvulus typically presents with progressive abdominal pain, nausea, and constipation and eventually results in bowel obstruction (eg, failure to pass gas, obstipation, possible perforation). Symptoms occur over the course of days, not months.

### **Educational objective:**

Constipation is a common adverse effect of non-dihydropyridine calcium channel blockers (eg, diltiazem, verapamil). Other medications that cause constipation include opiates, 5-HT<sub>3</sub> antagonists, iron tablets, aluminum-containing antacids, and medications with anticholinergic properties.

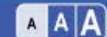
### **References**



A 34-year-old man is evaluated for several months of epigastric pain that is worse at night and is relieved by eating. The patient has no significant medical history and takes no medications. He does not use tobacco, alcohol, or illicit drugs. The patient immigrated to the United States from China 4 years ago. Vital signs are within normal limits. Physical examination shows mild epigastric tenderness to deep palpation. Upper gastrointestinal endoscopy reveals a 1-cm ulcer in the first portion of the duodenum. Additional testing is pending. In addition to proton pump inhibitor therapy, which of the following therapies would most likely prevent ulcer recurrence in this patient?

- ☐ A. Antibiotics
- ☐ B. Gastric cytoprotectants
- ☐ C. Glucocorticoids
- ☐ D. Histamine 2 receptor blockers
- ☐ E. Prokinetic agents
- ☐ F. Prostaglandin analogues





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- ☒ A. Antibiotics (80%)
- ☐ B. Gastric cytoprotectants (2%)
- ☐ C. Glucocorticoids (0%)
- ☐ D. Histamine 2 receptor blockers (9%)
- ☐ E. Prokinetic agents (0%)
- ☐ F. Prostaglandin analogues (6%)

Correct

80%

Answered correctly



43 secs

Time spent



08/26/2020

Last updated

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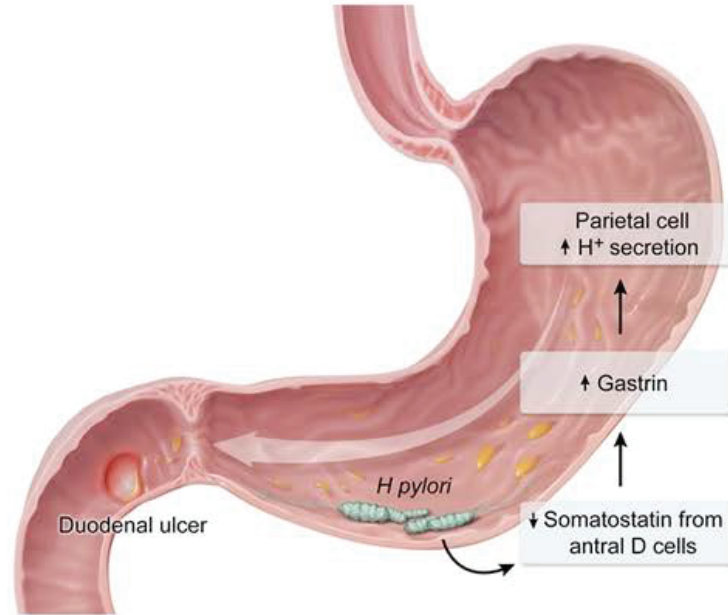


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Exhibit Display

*Helicobacter pylori* and duodenal ulcers



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This patient's symptoms and endoscopic findings are consistent with **duodenal peptic ulcer disease** (PUD). Up to 90% of duodenal ulcers are caused by ***Helicobacter pylori*** infection. The remaining cases are typically associated with nonsteroidal anti-inflammatory drug (NSAID) use, which is unlikely in this patient who takes no medications. Over 50% of the world population is colonized with *H pylori*, with a particularly high prevalence in resource-limited countries, including much of Africa, Western Asia, and South America.

To reduce the likelihood of PUD recurrence after ulcer healing, *H pylori* infection must be eradicated. Effective regimens typically involve a combination of **antibiotics** (eg, tetracycline, metronidazole) and proton pump inhibitors (eg, omeprazole), often with bismuth subsalicylate (ie, quadruple therapy). The antibiotic regimen can be tailored based on local resistance patterns.

**(Choice B)** Gastric cytoprotectants (eg, sucralfate) bind to the base of mucosal ulcers and protect them against gastric acid. This can help duodenal ulcers heal but would be less effective in preventing ulcer recurrence than eradication of *H pylori*.

**(Choice C)** Glucocorticoids should be avoided in patients with PUD as they can promote peptic ulcer formation, especially when combined with NSAIDs.





**(Choice C)** Glucocorticoids should be avoided in patients with PUD as they can promote peptic ulcer formation, especially when combined with NSAIDs.

**(Choice D)** Proton pump inhibitors suppress gastric acid secretion to a greater extent than histamine H<sub>2</sub>-receptor blockers (eg, ranitidine), allowing for superior ulcer healing during PUD treatment. However, neither medication would prevent ulcer recurrence (which requires *H pylori* eradication).

**(Choice E)** Metoclopramide is a dopamine antagonist with prokinetic and antiemetic properties that can be used to treat gastrointestinal motility disorders (eg, gastroparesis) and nausea/vomiting; however, it does not have a significant effect on PUD.

**(Choice F)** Prostaglandin analogues such as misoprostol are used to prevent NSAID-induced peptic ulcers.

**Educational objective:**

Most duodenal peptic ulcers are caused by *Helicobacter pylori* infection. The most effective method to prevent disease recurrence is to eradicate the infection with antibiotics (eg, tetracycline, metronidazole), typically in combination with proton pump inhibitors (eg, omeprazole) and, often, bismuth subsalicylate (quadruple therapy).







A 21-year-old Caucasian male presents to your office with mild jaundice after a hiking trip. He had a similar episode two years ago after fasting for five days. His physical examination is unremarkable except for mild jaundice.

### Liver studies

Albumin	4.2 mg/dL
Total protein, serum	6.8 g/dL
Total bilirubin	2.8 mg/dL
Direct bilirubin	0.2 mg/dL
Alkaline phosphatase	90 U/L
Aspartate aminotransferase (SGOT)	26 U/L





## Liver studies

Albumin	4.2 mg/dL
Total protein, serum	6.8 g/dL
Total bilirubin	2.8 mg/dL
Direct bilirubin	0.2 mg/dL
Alkaline phosphatase	90 U/L
Aspartate aminotransferase (SGOT)	26 U/L
Alanine aminotransferase (SGPT)	32 U/L

This patient most likely suffers from:





Aspartate aminotransferase

26 U/L

(SGOT)

Alanine aminotransferase

32 U/L

(SGPT)

This patient most likely suffers from:

- ☐ A. Gilbert syndrome
- ☐ B. Dubin-Johnson syndrome
- ☐ C. Acute viral hepatitis B
- ☐ D. Acute viral hepatitis C
- ☐ E. Acute alcoholic hepatitis
- ☐ F. Wilson's disease

**Submit**





Aspartate aminotransferase

(SGOT)

26 U/L

Alanine aminotransferase

(SGPT)

32 U/L

This patient most likely suffers from:

- ☒ A. Gilbert syndrome (81%)
- ☐ B. Dubin-Johnson syndrome (11%)
- ☐ C. Acute viral hepatitis B (2%)
- ☐ D. Acute viral hepatitis C (1%)
- ☐ E. Acute alcoholic hepatitis (1%)
- ☐ F. Wilson's disease (1%)

Correct



81%

Answered correctly



28 secs

Time spent



01/30/2021

Last updated

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The hepatic metabolism of bilirubin occurs in the following four stages: uptake from the bloodstream; storage within the hepatocyte; conjugation with glucuronic acid; and biliary excretion. In the normal individual, serum total bilirubin is 0.2-1 mg/dL, of which < 0.2 mg/dL is the direct fraction. Typically, elevated conjugated bilirubin levels are suggestive of hepatobiliary disease (eg, cirrhosis or hepatitis) because the bilirubin conjugates will reflux back into the plasma when the secretion of conjugated bilirubin into the bile is slowed. In contrast, elevated unconjugated bilirubin levels typically indicate increased bilirubin formation (such as that seen in hemolysis) or a slowing in bilirubin conjugation (such as that seen in this patient, who has Gilbert syndrome).

Gilbert syndrome is a common familial disorder of bilirubin glucuronidation in which the production of UDP glucuronyl transferases (enzymes that mediate glucuronidation of various substances) is reduced. Approximately 9% of individuals in Western countries are homozygous for this mutation, with another 30% heterozygous and asymptomatic. The diagnosis is suggested in those patients with no apparent liver disease who have mild unconjugated hyperbilirubinemia thought to be provoked by one of the classic triggers. Examples of such triggers include hemolysis, fasting, physical exertion, febrile illness, stress, and fatigue. Presumptive diagnosis can be made when the unconjugated hyperbilirubinemia persists with repeat testing, but liver function tests, complete blood count, blood smear, and reticulocyte count are



triggers. Examples of such triggers include hemolysis, fasting, physical exertion, febrile illness, stress, and fatigue. Presumptive diagnosis can be made when the unconjugated hyperbilirubinemia persists with repeat testing, but liver function tests, complete blood count, blood smear, and reticulocyte count are normal.

**(Choice B)** Individuals with the rare Dubin-Johnson syndrome have predominantly conjugated chronic hyperbilirubinemia that is not associated with hemolysis. For the diagnosis to be made, conjugated hyperbilirubinemia with a direct bilirubin fraction of at least 50% and an otherwise normal liver function profile must be present.

**(Choices C and D)** Expected laboratory findings in a patient with acute viral hepatitis include significant elevations in ALT and AST (with ALT > AST), followed by rises in bilirubin and alkaline phosphatase.

**(Choice E)** Alcoholic hepatitis is typically associated with a significant drinking history and is commonly characterized by an AST:ALT ratio greater than 2:1.

**(Choice F)** Wilson's disease is the likely diagnosis in a patient younger than 30 years old with unexplained chronic hepatitis (elevated AST and ALT). The presence of low serum ceruloplasmin and increased urinary copper excretion or Kayser-Fleischer rings provides diagnostic confirmation.

**Educational Objective:**





Mark

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Lab Values

Notes

Calculator

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Text Zoom

Settings

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### Educational Objective:

Gilbert syndrome is the likely diagnosis in patients with no apparent liver disease who have mild unconjugated hyperbilirubinemia that appears provoked by one of the classic triggers.

Pathology

Gastrointestinal &amp; Nutrition

Hereditary hyperbilirubinemias

Block Time Remaining: 00:23:18

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Feedback



Suspend



End Block



Mark



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Tutorial



Lab Values



Notes



Calculator



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Text Zoom



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A 46-year-old woman comes to the office due to dysphagia. The patient has had difficulty swallowing both liquids and solid foods as well as frequent episodes of regurgitation and cough while eating. She has also had weakness in her extremities and a rash. The patient has no prior medical problems and takes no medications. Vital signs are within normal limits. Physical examination shows an erythematous eruption on the upper eyelids. The oropharynx is clear and cardiopulmonary and abdominal examinations are unremarkable. She has difficulty lifting her arms above her head and standing from a sitting position. Which of the following is the most likely cause of this patient's dysphagia?

- ☐ A. Atrophy and fibrous replacement of the distal esophageal muscularis propria
- ☐ B. Diffuse eosinophil-predominant inflammation of the esophageal mucosa
- ☐ C. Inflammation and degeneration of the esophageal myenteric plexus
- ☐ D. Outpouching of hypopharyngeal mucosa through weakened muscle
- ☐ E. Perifascicular atrophy of muscle fibers in the proximal esophageal muscularis propria

**Submit**

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Suspend



End Block

A 46-year-old woman comes to the office due to dysphagia. The patient has had difficulty swallowing both liquids and solid foods as well as frequent episodes of regurgitation and cough while eating. She has also had weakness in her extremities and a rash. The patient has no prior medical problems and takes no medications. Vital signs are within normal limits. Physical examination shows an erythematous eruption on the upper eyelids. The oropharynx is clear and cardiopulmonary and abdominal examinations are unremarkable. She has difficulty lifting her arms above her head and standing from a sitting position. Which of the following is the most likely cause of this patient's dysphagia?

- ☐ A. Atrophy and fibrous replacement of the distal esophageal muscularis propria (24%)
- ☒ B. Diffuse eosinophil-predominant inflammation of the esophageal mucosa (7%)
- ☐ C. Inflammation and degeneration of the esophageal myenteric plexus (18%)
- ☐ D. Outpouching of hypopharyngeal mucosa through weakened muscle (2%)
- ☒ E. Perifascicular atrophy of muscle fibers in the proximal esophageal muscularis propria (46%)

Incorrect





This patient has painless **proximal muscle weakness**; in association with the heliotrope **rash** on her eyelids, this presentation is consistent with **dermatomyositis**, an inflammatory myopathy that primarily affects **striated muscle** and skin. Diagnostic findings include elevated muscle enzymes (eg, creatinine kinase) and positive autoantibodies (ie, antinuclear antibody [high sensitivity, low specificity], anti-Jo-1 [low sensitivity, high specificity]). Muscle biopsy in dermatomyositis shows perimysial inflammatory infiltrates and atrophy involving the fibers around the periphery of muscle fascicles (**perifascicular atrophy**).

The **oropharynx and upper esophagus** also contain skeletal muscle that can be affected in dermatomyositis and polymyositis, leading to **dysphagia** and pulmonary aspiration. Other important complications of inflammatory myopathies include interstitial lung disease and **myocarditis** (due to involvement of striated cardiac muscle).

**(Choice A)** Progressive systemic sclerosis (scleroderma) commonly affects the esophagus, leading to atrophy and fibrous replacement of the distal esophageal muscularis propria. Clinical features include dysphagia, reflux esophagitis, and aspiration. However, the dermal manifestations include sclerodactyly, digital ulcers, and calcinosis cutis, rather than a heliotrope rash. Also, dermatomyositis affects only the striated muscle in the oropharynx and upper esophagus (eg, choking, aspiration), whereas scleroderma can affect the lower esophagus.





can affect the lower esophagus.

**(Choice B)** Eosinophilic esophagitis typically presents with dysphagia, epigastric pain, recurrent esophageal reflux, and food impaction. Skin rash and extremity weakness would be unexpected.

**(Choice C)** Achalasia is caused by inflammation and degeneration of the esophageal myenteric plexus, resulting in impaired relaxation of the smooth muscle in the distal esophagus and lower esophageal sphincter. It typically presents with dysphagia, regurgitation, and heartburn but is not associated with rash or skeletal muscle weakness.

**(Choice D)** Zenker diverticulum develops immediately above the upper esophageal sphincter, with posterior mucosal herniation between the fibers of the cricopharyngeus muscle. Although it presents with dysphagia, regurgitation, and aspiration, it is not associated with rash or muscular weakness.

**Educational objective:**

Dermatomyositis is characterized by proximal muscle weakness resembling polymyositis, with additional inflammatory features affecting the skin (eg, heliotrope rash, Gottron papules). In both conditions, involvement of striated muscle in the oropharynx and heart can lead to dysphagia, pulmonary aspiration, and myocarditis.







A 45-year-old woman is brought to the emergency department with severe abdominal pain, fever, and confusion. The patient's husband reports that, yesterday, she began to have worsening right-sided abdominal pain associated with nausea and several episodes of vomiting. This morning, she has been slow to respond and is confused about where she is. The patient has a history of depression and takes sertraline. Temperature is 39.5 C (103.1 F), blood pressure is 88/50 mm Hg, pulse is 104/min, and respirations are 26/min. She appears ill and confused, and the sclera are icteric. Abdominal examination demonstrates significant tenderness with guarding in the right upper quadrant. Which of the following is the most likely underlying cause of this patient's current condition?

- ☐ A. Acinar cell dysfunction and necrosis
- ☐ B. Calculous obstruction of the common bile duct
- ☐ C. Extensive hepatic formation of noncaseating granulomas
- ☐ D. Immune-mediated destruction of hepatocytes
- ☐ E. Medication overdose with hepatic failure
- ☐ F. Neoplastic mass in the pancreatic tail







abdominal pain associated with nausea and several episodes of vomiting. This morning, she has been slow to respond and is confused about where she is. The patient has a history of depression and takes sertraline. Temperature is 39.5 C (103.1 F), blood pressure is 88/50 mm Hg, pulse is 104/min, and respirations are 26/min. She appears ill and confused, and the sclera are icteric. Abdominal examination demonstrates significant tenderness with guarding in the right upper quadrant. Which of the following is the most likely underlying cause of this patient's current condition?

- ☐ A. Acinar cell dysfunction and necrosis (4%)
- ☒ B. Calculous obstruction of the common bile duct (57%)
- ☐ C. Extensive hepatic formation of noncaseating granulomas (1%)
- ☐ D. Immune-mediated destruction of hepatocytes (6%)
- ☐ E. Medication overdose with hepatic failure (29%)
- ☐ F. Neoplastic mass in the pancreatic tail (0%)

Omitted

Correct answer



57%

Answered correctly



01 min, 24 secs

Time spent



10/20/2020

Last updated

Block Time Remaining: 00:26:30

TUTOR

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1



Feedback



Suspend



End Block



Mark



Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

## Acute cholangitis

<b>Etiology</b>	<ul style="list-style-type: none"><li>• Ascending infection due to biliary obstruction<ul style="list-style-type: none"><li>◦ Obstructive gallstone</li><li>◦ Malignancy (eg, cholangiocarcinoma, pancreatic head cancer)</li><li>◦ Stricture (eg, primary sclerosing cholangitis)</li><li>◦ Biliary stent blockage</li></ul></li></ul>
<b>Clinical presentation</b>	<ul style="list-style-type: none"><li>• Fever, jaundice, RUQ pain (Charcot triad)</li><li>• <math>\pm</math> Hypotension, altered mental status (Reynolds pentad)</li></ul>
<b>Laboratory results</b>	<ul style="list-style-type: none"><li>• Cholestatic liver function test<ul style="list-style-type: none"><li>◦ <math>\uparrow</math> Alkaline phosphatase, bilirubin</li><li>◦ <math>\pm</math> Mildly elevated transaminases</li></ul></li><li>• Leukocytosis</li></ul>
<b>Imaging</b>	<ul style="list-style-type: none"><li>• Biliary dilation on abdominal imaging</li></ul>

**RUQ** = right upper quadrant.



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

This patient with fever, right upper quadrant (RUQ) pain, jaundice, confusion, and hypotension has **acute cholangitis (AC)**. AC is a life-threatening infection that typically develops in the setting of **biliary obstruction**, which enables bacteria to proliferate within the biliary tree. Obstruction can occur in a variety of settings (eg, malignant biliary obstruction, biliary stricture) but is most commonly caused by a **calculous obstruction of the common bile duct** (ie, choledocholithiasis).

AC is characterized by **fever, RUQ pain**, and **jaundice** (Charcot triad); **hypotension** and **altered mental status** (Reynold pentad) occur in severe cases. Laboratory findings include leukocytosis, direct hyperbilirubinemia, and elevated alkaline phosphatase. Abdominal imaging (eg, ultrasound) demonstrates common bile duct dilation, possibly with evidence of an obstructing stone. Management includes antibiotics, intravenous fluid resuscitation, and endoscopic or percutaneous techniques to relieve the biliary obstruction.

**(Choice A)** Acute pancreatitis is characterized by acinar cell dysfunction and necrosis. Although patients can develop fever and hypotension, typical manifestations include epigastric pain radiating into the back, nausea/vomiting, and elevated lipase. Jaundice is unexpected unless a gallstone obstructs both the common bile and the pancreatic ducts, resulting in simultaneous AC.

**(Choice C)** Hepatic sarcoidosis, which causes extensive noncaseating granuloma formation in the liver



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice C)** Hepatic sarcoidosis, which causes extensive noncaseating granuloma formation in the liver, can present with cholestasis (eg, elevated alkaline phosphatase, jaundice, pruritus) and hepatomegaly. However, sepsis, hypotension, and confusion are unexpected, and most patients have evidence of systemic sarcoidosis (eg, hilar adenopathy, cough).

**(Choice D)** Autoimmune hepatitis causes immune-mediated hepatocyte destruction and usually presents with asymptomatic transaminitis or the insidious onset of fatigue and anorexia. Fever, tachycardia, and hypotension are unexpected and more consistent with infection due to AC.

**(Choice E)** Acetaminophen overdose can cause RUQ pain, jaundice, vomiting, and confusion, typically around 72 hours after ingestion. However, fever is atypical and more consistent with AC.

**(Choice F)** Although a mass in the pancreatic head can cause biliary obstruction, pancreatic tail masses are not located near the biliary tree and therefore are not usually associated with AC. They more commonly present with epigastric abdominal pain and weight loss.

### Educational objective:

Acute cholangitis is a life-threatening infection characterized by fever, right upper quadrant pain, and jaundice (Charcot triad); hypotension and altered mental status (Reynold pentad) occur in severe cases.

Acute cholangitis typically develops in the setting of biliary obstruction; common etiologies include



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice D)** Autoimmune hepatitis causes immune-mediated hepatocyte destruction and usually presents with asymptomatic transaminitis or the insidious onset of fatigue and anorexia. Fever, tachycardia, and hypotension are unexpected and more consistent with infection due to AC.

**(Choice E)** Acetaminophen overdose can cause RUQ pain, jaundice, vomiting, and confusion, typically around 72 hours after ingestion. However, fever is atypical and more consistent with AC.

**(Choice F)** Although a mass in the pancreatic head can cause biliary obstruction, pancreatic tail masses are not located near the biliary tree and therefore are not usually associated with AC. They more commonly present with epigastric abdominal pain and weight loss.

### Educational objective:

Acute cholangitis is a life-threatening infection characterized by fever, right upper quadrant pain, and jaundice (Charcot triad); hypotension and altered mental status (Reynold pentad) occur in severe cases. Acute cholangitis typically develops in the setting of biliary obstruction; common etiologies include gallstones, malignancy, and strictures.

Pathology

Subject

Gastrointestinal &amp; Nutrition

System

Cholangitis

Topic



1



Feedback



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End Block



A 38-year-old man comes to the emergency department with severe abdominal pain and vomiting. The pain radiates to his back and improves by bending forward. Physical examination shows tenderness over the epigastrium and decreased bowel sounds. The patient is admitted to the hospital and treated with intravenous fluids and pain medication, but his condition fails to improve. An abdominal CT scan reveals diffuse pancreatic enlargement with areas of necrosis. The inappropriate activation of which of the following most likely initiated this patient's condition?

- ☐ A. Amylase
- ☐ B. Chymotrypsinogen
- ☐ C. Lipase
- ☐ D. Proelastase
- ☐ E. Prophospholipase
- ☐ F. Trypsinogen

**Submit**

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Feedback

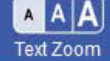
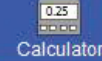
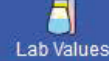
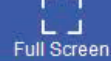


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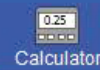
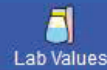




A 38-year-old man comes to the emergency department with severe abdominal pain and vomiting. The pain radiates to his back and improves by bending forward. Physical examination shows tenderness over the epigastrium and decreased bowel sounds. The patient is admitted to the hospital and treated with intravenous fluids and pain medication, but his condition fails to improve. An abdominal CT scan reveals diffuse pancreatic enlargement with areas of necrosis. The inappropriate activation of which of the following most likely initiated this patient's condition?

- ☐ A. Amylase (3%)
- ☐ B. Chymotrypsinogen (3%)
- ☐ C. Lipase (12%)
- ☐ D. Proelastase (1%)
- ☐ E. Prophospholipase (0%)
- ☒ F. Trypsinogen (78%)





## Exhibit Display

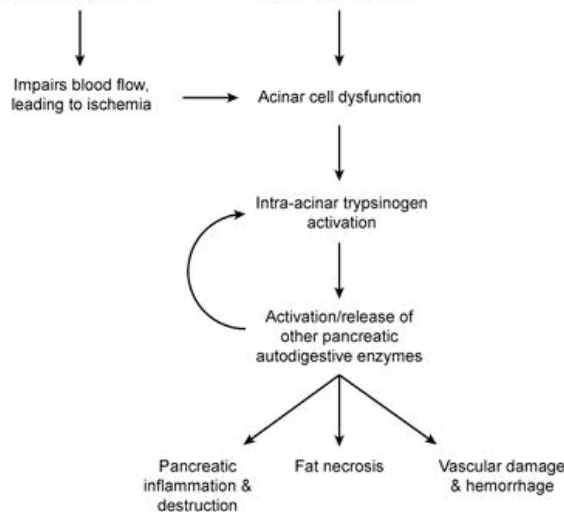
## Pathogenesis of acute pancreatitis

## Ductal obstruction

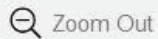
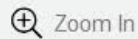
- Ampullary obstruction (eg, gallstones, tumors)
- Ductal concretions due to chronic alcoholism

## Direct parenchymal injury

- Alcohol
- Iatrogenic (eg, drugs & post-ERCP)
- Hypertriglyceridemia



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Mark

Previous

Next

inflammation &  
destruction

Full Screen



Tutorial



Lab Values



Notes



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Most **pancreatic enzymes** are synthesized by pancreatic acinar cells as inactive enzyme precursors called zymogens. Zymogen granules are secreted from the apical surface of acinar cells into the lumen. After traversing the pancreatic duct system, they drain through the ampulla of Vater into the descending part of the duodenum. The enzyme enterokinase (secreted from intestinal mucosa) cleaves trypsinogen into trypsin, its active form. Once a small quantity of trypsin is produced, it activates other zymogens, including chymotrypsin, elastase, and carboxypeptidase, through proteolytic cleavage. Trypsin can also cleave trypsinogen to produce more trypsin, accelerating pancreatic enzyme activation in the duodenum.

The pathogenesis of **acute pancreatitis** begins with either a toxic or an ischemic injury to the acinar cells that leads to **premature activation of trypsin** inside the pancreatic acini. Trypsin then activates the other proteolytic enzymes and starts a self-sustaining cycle of pancreatic inflammation and autodigestion with further release of digestive enzymes. In severe cases, this process can result in **necrotizing pancreatitis**, which is characterized by gross areas of parenchymal necrosis with a high propensity for secondary bacterial infection.

**(Choice A)** Amylase hydrolyzes starch to produce maltose (a glucose-glucose disaccharide) and trisaccharide maltotriose and limit dextrins. It does not require activation by trypsin.



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Previous



Next



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Lab Values



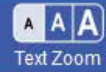
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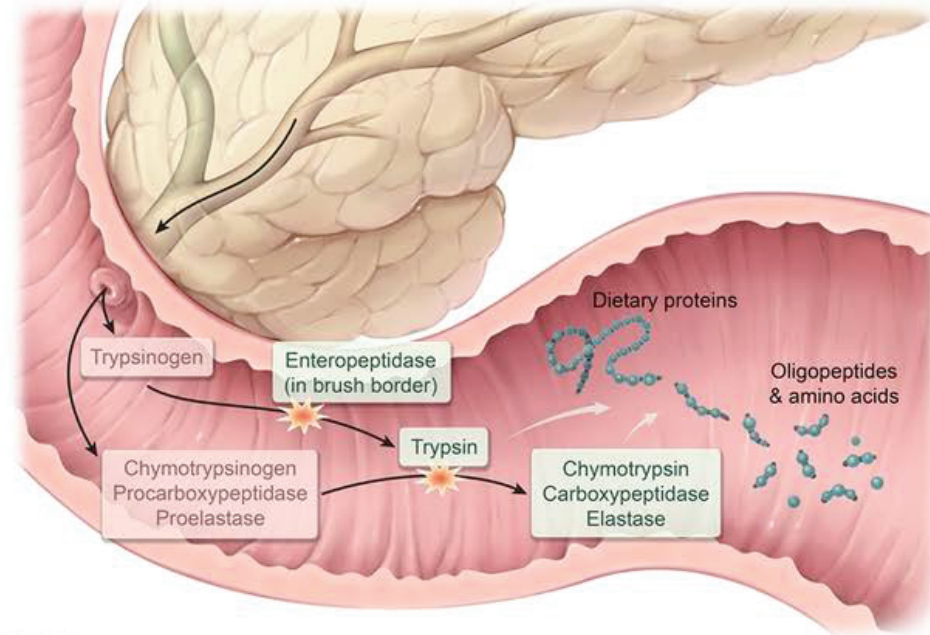
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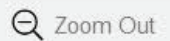
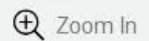
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### Exhibit Display

## Pancreatic enzyme activation



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



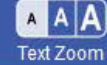
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Text Zoom



Settings

bacterial infection.

**(Choice A)** Amylase hydrolyzes starch to produce maltose (a glucose-glucose disaccharide) and trisaccharide maltotriose and limit dextrins. It does not require activation by trypsin.

**(Choices B, D, and E)** Chymotrypsin, phospholipase A2 (which can damage cell membranes), and elastase are secreted by the pancreas as inactive precursors (chymotrypsinogen, prophospholipase A2, and proelastase) that are subsequently activated by trypsin.

**(Choice C)** Lipase hydrolyzes triglycerides into fatty acids and glycerol. It does not require activation by trypsin (although its activity is increased by colipase, which is activated by trypsin). Release of lipase during acute pancreatitis causes the formation of characteristic calcium soap deposits (fat necrosis).

### Educational objective:

Pancreatic zymogens are normally converted into their active form by trypsin in the duodenal lumen.

Premature cleavage of trypsinogen to trypsin within the pancreas leads to uncontrolled activation of these zymogens, causing pancreatic autodigestion and acute pancreatitis.

Pathophysiology  
Subject

Gastrointestinal & Nutrition  
System

Acute pancreatitis  
Topic



0



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 4-day-old newborn is brought to the office for a 2-day history of progressive jaundice. He was born at term following an uncomplicated vaginal delivery. The patient has been breastfed since birth. Vital signs are normal. Examination shows scleral icterus and jaundice from the face to the upper abdomen.

Laboratory results are as follows:

Complete blood count

Hematocrit 52%

Reticulocytes 1%

Liver function studies

Total bilirubin 10.3 mg/dL

Direct bilirubin 0.7 mg/dL

Aspartate aminotransferase (SGOT) 18 U/L

Alanine aminotransferase (SGPT) 24 U/L

Which of the following is the most likely explanation for these findings?







Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

## Liver function studies

Total bilirubin 10.3 mg/dL

Direct bilirubin 0.7 mg/dL

Aspartate aminotransferase (SGOT) 18 U/L

Alanine aminotransferase (SGPT) 24 U/L

Which of the following is the most likely explanation for these findings?

- ☐ A. CD8<sup>+</sup> T-lymphocyte-mediated hepatocellular injury
- ☐ B. Decreased intestinal beta-glucuronidase activity
- ☐ C. Deficiency of erythrocyte glucose-6-phosphate dehydrogenase
- ☒ D. Deficiency of hepatic UDP glucuronosyltransferase activity
- ☐ E. Fibrous obliteration of the extrahepatic biliary tree

Submit





Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

## Liver function studies

Total bilirubin 10.3 mg/dL

Direct bilirubin 0.7 mg/dL

Aspartate aminotransferase (SGOT) 18 U/L

Alanine aminotransferase (SGPT) 24 U/L

Which of the following is the most likely explanation for these findings?

- ☐ A. ~~CD8<sup>+</sup> T-lymphocyte-mediated hepatocellular injury~~ (0%)
- ☐ B. Decreased intestinal beta-glucuronidase activity (9%)
- ☐ C. ~~Deficiency of erythrocyte glucose-6-phosphate dehydrogenase~~ (2%)
- ☒ D. Deficiency of hepatic UDP glucuronosyltransferase activity (83%)
- ☐ E. ~~Fibrous obliteration of the extrahepatic biliary tree~~ (4%)

Correct



83%

Answered correctly



01 min, 22 secs

Time spent



02/11/2021

Last updated

Block Time Remaining: 00:28:23

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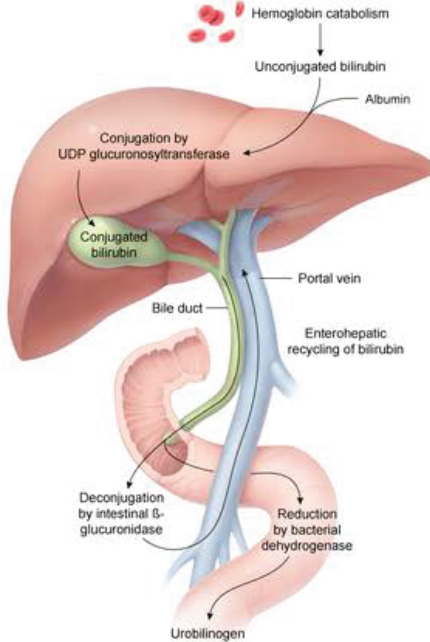
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End Block

### Exhibit Display

#### Bilirubin metabolism



Zoom In

Zoom Out

Reset

New | Existing

My Notebook





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This neonate most likely has **benign neonatal hyperbilirubinemia**, a **physiologic** condition characterized by an **elevated indirect bilirubin** level that peaks at **age 2-5 days**.

The pathophysiology of benign neonatal hyperbilirubinemia includes the following:

- **↑ Bilirubin production:** Fetal red blood cells (RBCs) are increased in number and have a shorter life span compared to RBCs in children and adults. Physiologic breakdown of these RBCs causes excess production of indirect bilirubin.
- **↓ Bilirubin clearance:** Physiologically **decreased** levels of hepatic uridine diphosphogluconate (**UDP**) **glucuronosyltransferase** in newborns results in decreased bilirubin conjugation and excretion into the bile.
- **↑ Enterohepatic circulation:** In the colon, conjugated bilirubin is deconjugated by intestinal beta-glucuronidase. Lack of bacterial enzymes due to the relative sterility of the newborn gut results in decreased metabolism of unconjugated bilirubin to urobilinogen, thereby allowing unconjugated bilirubin to be reabsorbed via enterohepatic circulation (**Choice B**).

Benign neonatal hyperbilirubinemia is typically asymptomatic except for scleral icterus and **jaundice**. The resolution of benign neonatal hyperbilirubinemia is expected by age 1-2 weeks as UDP



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Suspend



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Benign neonatal hyperbilirubinemia is typically asymptomatic except for scleral icterus and jaundice. The resolution of benign neonatal hyperbilirubinemia is expected by age 1-2 weeks as UDP glucuronosyltransferase activity and gut bacteria increase, allowing increased bilirubin clearance and excretion.

**(Choice A)** Viral hepatitis (eg, hepatitis B or C) results in CD8<sup>+</sup> T-lymphocyte-mediated hepatocellular injury and jaundice. However, vertical transmission of hepatitis viruses does not cause symptoms in the neonatal period. Moreover, once the patient is symptomatic, transaminases would be elevated.

**(Choice C)** Glucose-6-phosphate dehydrogenase deficiency can present with jaundice and indirect hyperbilirubinemia in the early neonatal period. However, because hemolysis contributes to the pathophysiology of jaundice in this condition, the hematocrit would be decreased and the reticulocyte count would be elevated.

**(Choice E)** Biliary atresia is characterized by fibrous obliteration of the extrahepatic biliary tree and typically presents with jaundice in the first 2 months of life. However, direct bilirubin is elevated due to biliary tract obstruction. In addition, patients often have acholic stools and dark urine.

**Educational objective:**





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

## Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

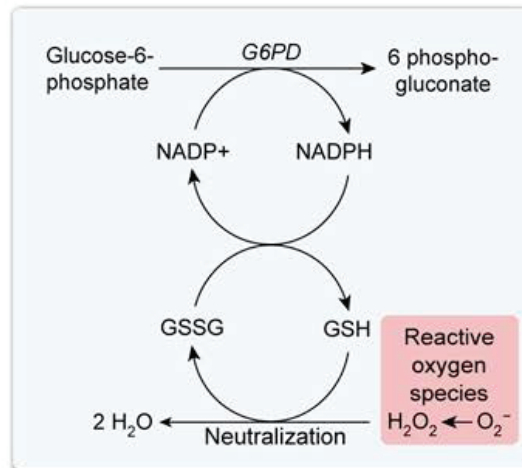
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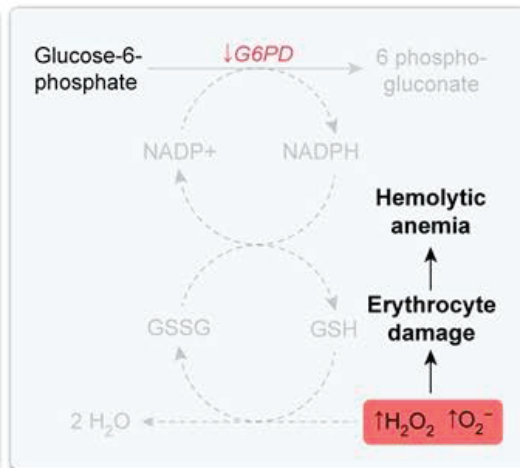


## Exhibit Display

## Normal

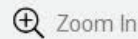


## G6PD deficiency

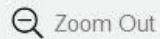


G6PD = glucose-6-phosphate dehydrogenase; GSH = glutathione; GSSG = glutathione disulfide.

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Zoom Out



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Feedback



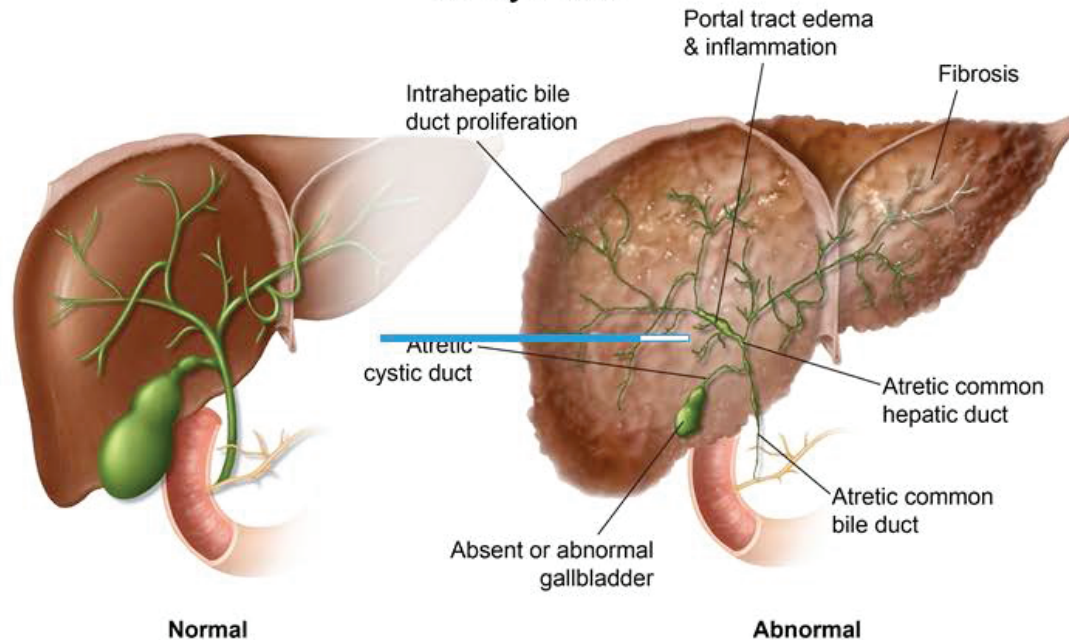
Suspend



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## Exhibit Display

## Biliary atresia



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New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

injury and jaundice. However, vertical transmission of hepatitis viruses does not cause symptoms in the neonatal period. Moreover, once the patient is symptomatic, transaminases would be elevated.

**(Choice C)** [Glucose-6-phosphate dehydrogenase deficiency](#) can present with jaundice and indirect hyperbilirubinemia in the early neonatal period. However, because hemolysis contributes to the pathophysiology of jaundice in this condition, the hematocrit would be decreased and the reticulocyte count would be elevated.

**(Choice E)** [Biliary atresia](#) is characterized by fibrous obliteration of the extrahepatic biliary tree and typically presents with jaundice in the first 2 months of life. However, direct bilirubin is elevated due to biliary tract obstruction. In addition, patients often have acholic stools and dark urine.

### Educational objective:

Benign neonatal hyperbilirubinemia presents with jaundice and elevated indirect bilirubin levels that peak at age 2-5 days. Pathophysiology includes impaired bilirubin clearance by the liver due to decreased hepatic UDP glucuronosyltransferase, an enzyme responsible for bilirubin conjugation.

### References

- [Neonatal jaundice.](#)
- [Neonatal jaundice.](#)



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Feedback



Suspend



End Block





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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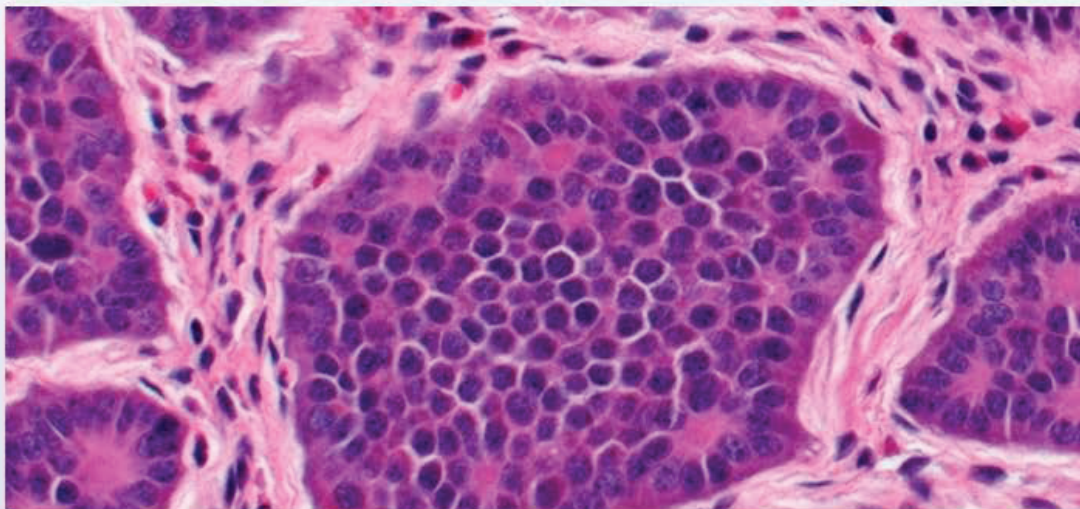


Text Zoom



Settings

A 38-year-old woman comes to the hospital with 4 hours of abdominal pain, nausea, and vomiting. Her pain started in the periumbilical area and is now localized to the right lower quadrant. Temperature is 38.3 C (101 F). On examination, the patient has right lower quadrant tenderness with guarding. An appendectomy is performed, and light microscopy of the appendix shows infiltrating neutrophils in the muscularis propria, consistent with the diagnosis of acute appendicitis. Further evaluation reveals abnormal islands of small cells, as shown in the image below.



1



Feedback



Suspend



End Block



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Previous



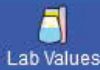
Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

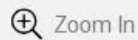
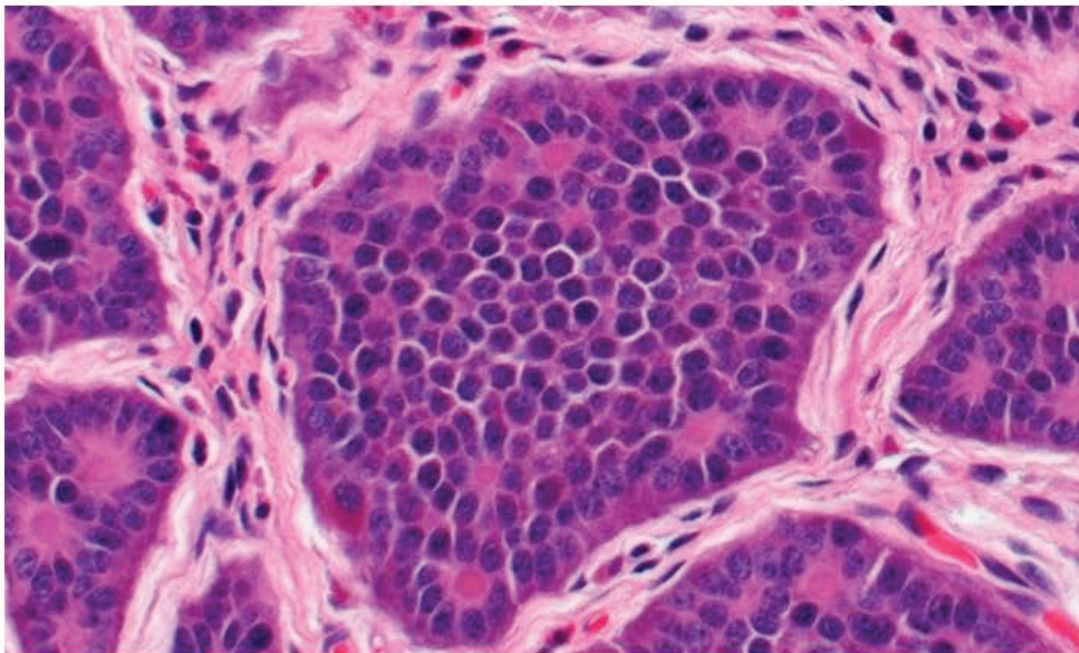


Text Zoom

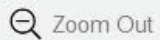


Settings

## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



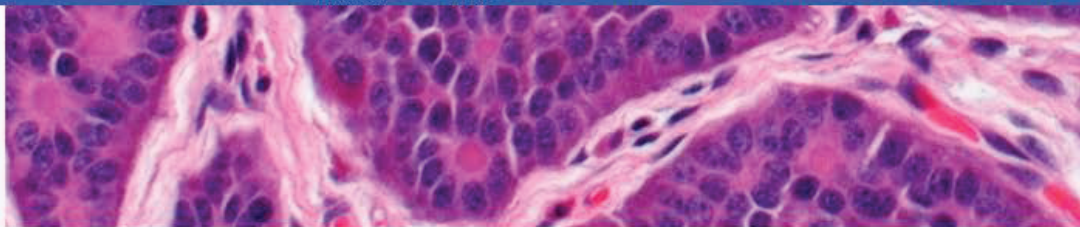
Reverse Color



Text Zoom



Settings



These cells are most likely derived from which of the following sources?

- ☐ A. Connective tissue
- ☐ B. Hematopoietic cells
- ☐ C. Intestinal mucus-secreting cells
- ☐ D. Neuroendocrine cells
- ☐ E. Smooth muscle cells
- ☐ F. Vascular endothelium

Submit



1



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

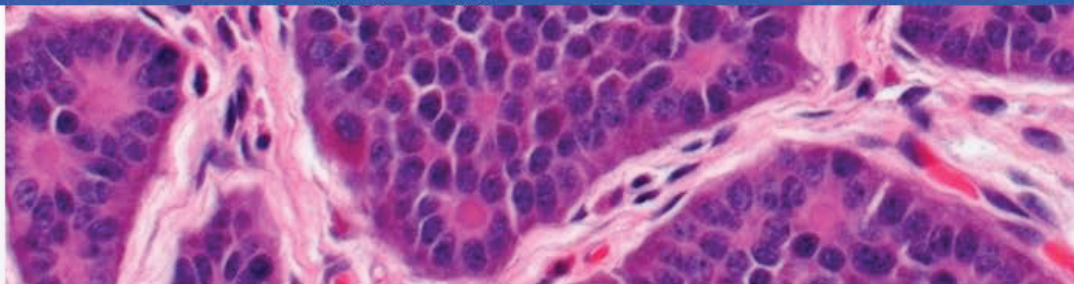
Notes

Calculator

Reverse Color

Text Zoom

Settings



These cells are most likely derived from which of the following sources?

- ☐ A. Connective tissue (2%)
- ☐ B. Hematopoietic cells (12%)
- ☐ C. Intestinal mucus-secreting cells (13%)
- ☒ D. Neuroendocrine cells (66%)
- ☐ E. Smooth muscle cells (2%)
- ☐ F. Vascular endothelium (2%)



1



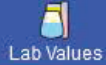
Feedback



Suspend



End Block



## Explanation

The image shows the typical microscopic appearance of a **carcinoid tumor**. Note the **uniformity** in shape and size of the cells that comprise the **islands**. Trabeculae, glands, strands, or sheets of cells may also be formed. Tumor cells have an **eosinophilic** cytoplasm and **oval-to-round** stippled nuclei. On electron microscopy, multiple dense-core granules are seen in the cytoplasm; these contain secretory products such as vasoactive molecules (eg, serotonin, bradykinin, histamine) and hormones (eg, gastrin).

Carcinoid tumors are malignant transformations of **neuroendocrine cells**, most commonly located in the gastrointestinal tract (eg, small intestine, rectum, appendix), followed by the bronchopulmonary system. The majority of appendiceal carcinoids have a benign clinical course. They are usually found at the tip of the appendix in asymptomatic patients who have undergone appendectomy for unrelated reasons. Tumors at the base of the appendix may cause obstruction and **appendicitis**. In rare cases, large tumors will metastasize to the liver, causing carcinoid syndrome (flushing, diarrhea, bronchospasm).

**(Choice A)** Connective tissue can be a source of both benign (**fibromas**) and malignant (**fibrosarcomas**) tumors.

**(Choice B)** Abnormal proliferation of hematopoietic cells leads to a variety of myeloid and lymphoid neoplasms.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



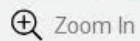
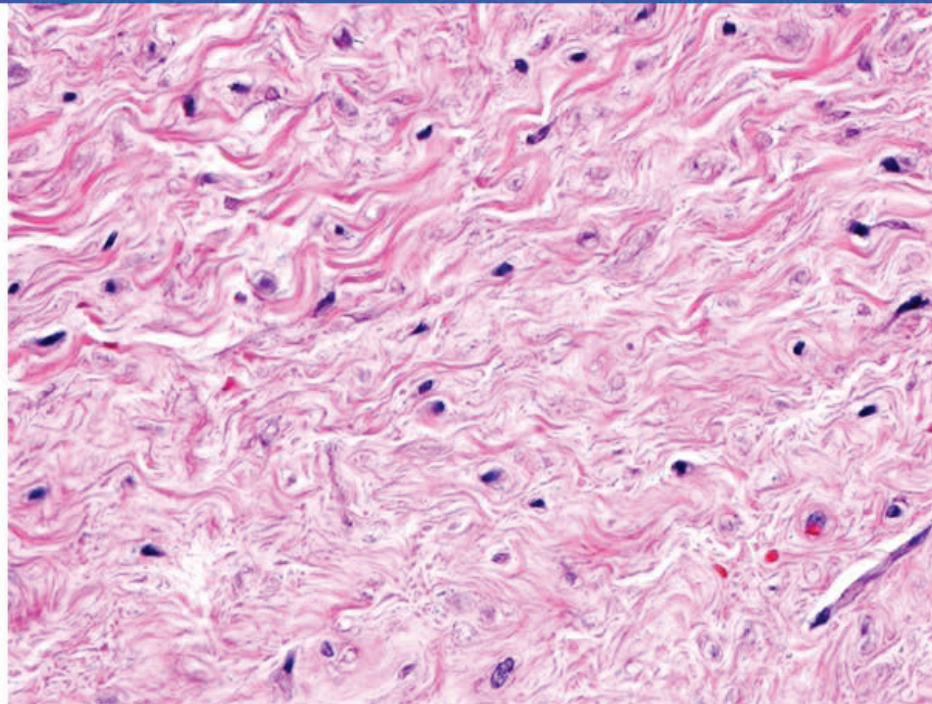
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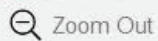
Settings

Explanation

## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook

neoplasms.

Block Time Remaining: 00:29:43

TUTOR

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



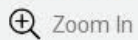
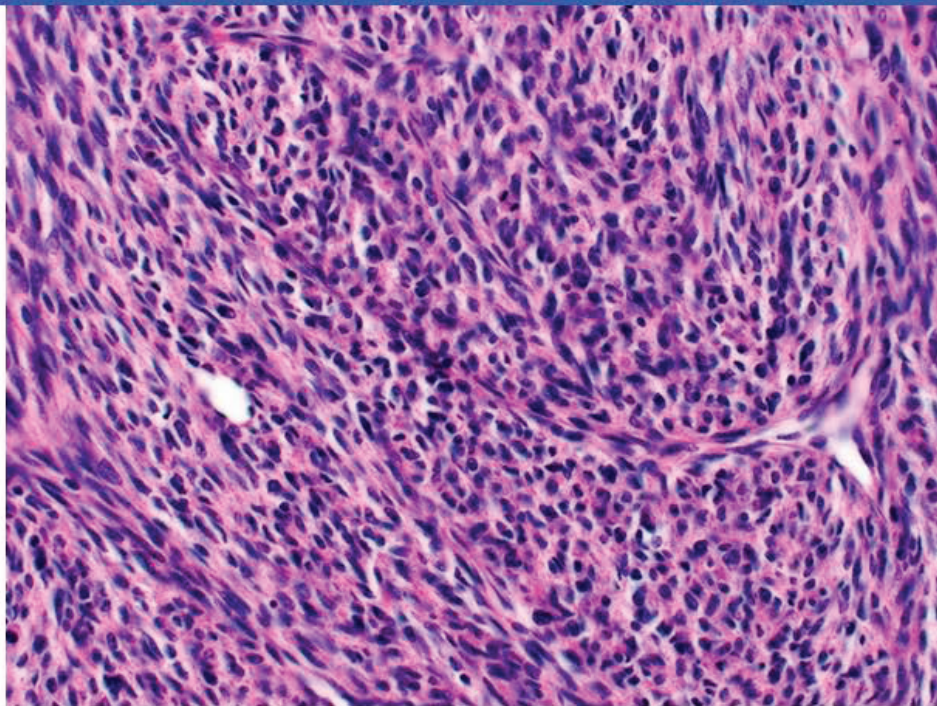
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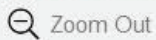
Settings

Explanation

## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook

neoplasms.

Block Time Remaining: 00:29:43

TUTOR

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

tumors.

**(Choice B)** Abnormal proliferation of hematopoietic cells leads to a variety of myeloid and lymphoid neoplasms.

**(Choice C)** Intestinal epithelial cells (both absorptive and mucus-secreting) can give rise to [intestinal adenocarcinomas](#).

**(Choice E)** Smooth muscle cells give rise to [leiomyomas](#) and [leiomyosarcomas](#).

**(Choice F)** Vascular endothelial cells can be a source of benign (hemangioma), intermediate (hemangioendothelioma), and malignant ([angiosarcoma](#)) tumors.

### Educational objective:

Carcinoid tumors are composed of islands or sheets of uniform cells with eosinophilic cytoplasm and oval-to-round stippled nuclei. These tumors are often derived from neuroendocrine cells in the gastrointestinal tract. Appendiceal carcinoids typically have a benign course but may cause appendicitis or, rarely, carcinoid syndrome (eg, with liver metastasis).

### References

- [Updated population-based review of carcinoid tumors.](#)



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



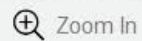
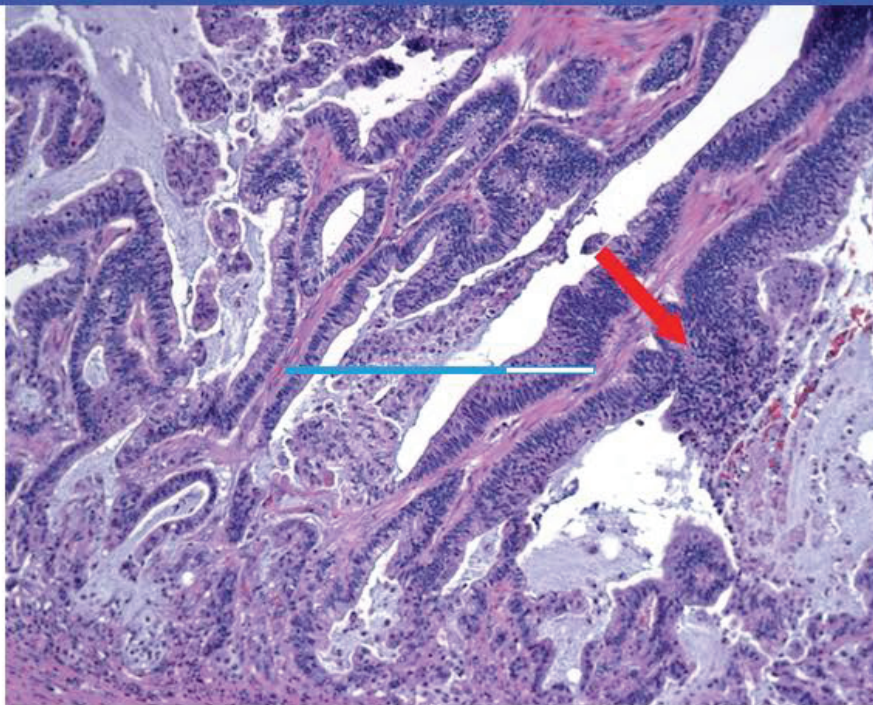
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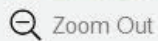
Settings

tumors

## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



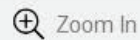
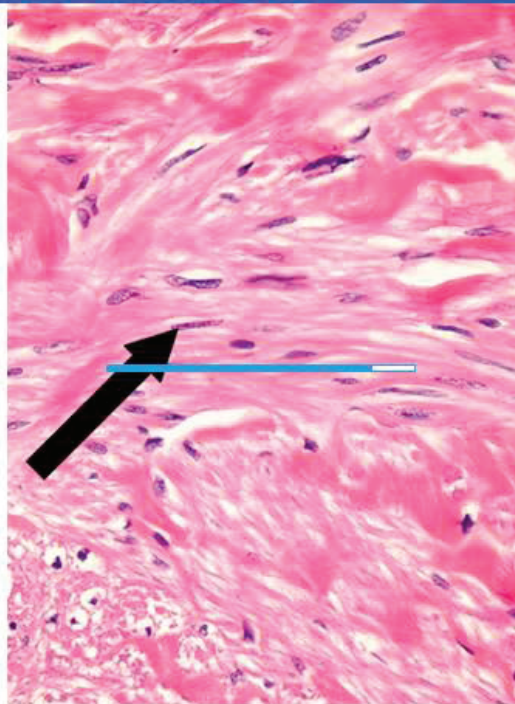
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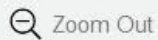
Settings

tumors

## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



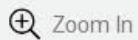
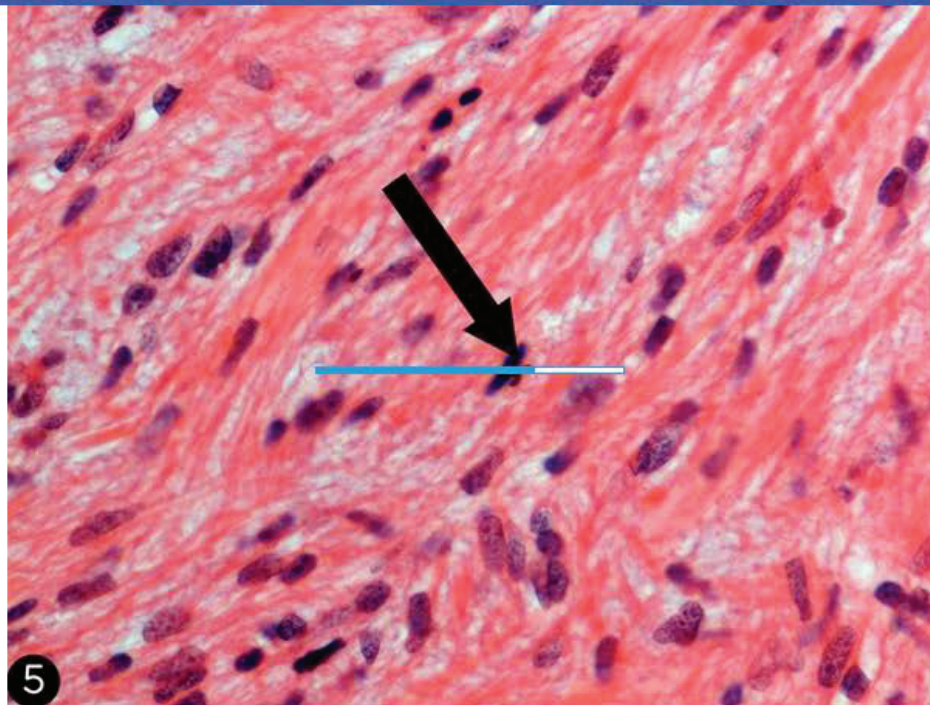
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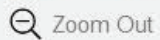
Settings

tumors

## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



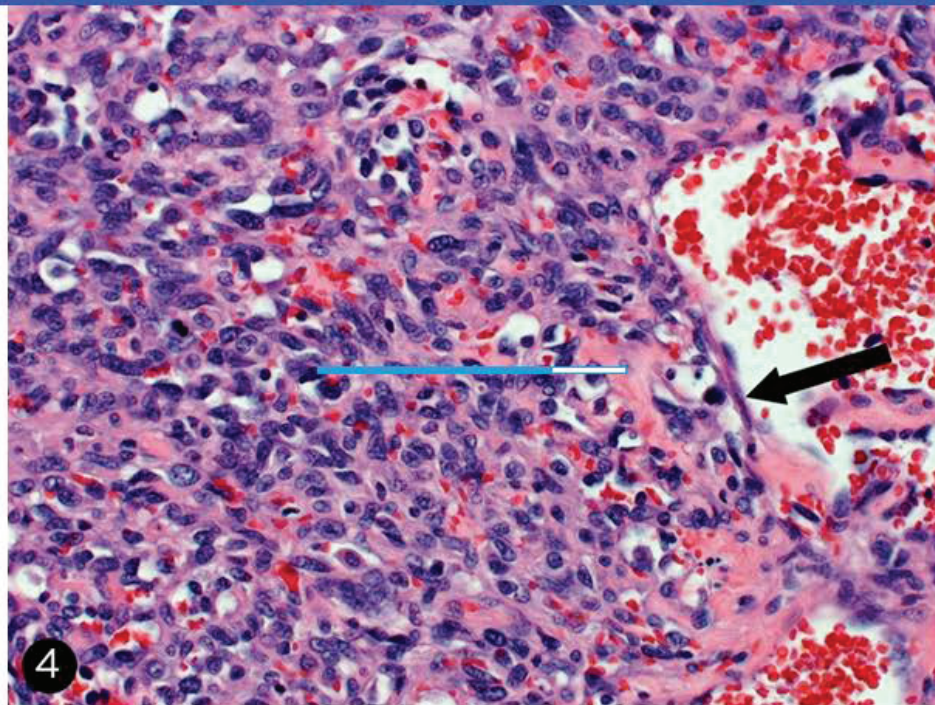
Text Zoom



Settings

tumors

## Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



1



Feedback



Suspend



End Block





Previous



Next



Full Screen



Tutorial



Lab Values



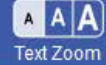
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 75-year-old man is brought to the emergency department due to acute-onset profuse vomiting of large amounts of bright red blood. He has had intermittent, dull epigastric pain for the last 3 months. Medical history is significant for chronic obstructive pulmonary disease with multiple exacerbations and lumbar spinal stenosis. The patient has smoked 1 pack of cigarettes daily for 40 years. Blood pressure is 70/40 mm Hg and pulse is 120/min. Examination shows epigastric tenderness. The patient dies an hour after admission despite resuscitation efforts. Autopsy shows a deep peptic ulcer localized proximally on the lesser curvature of the stomach. The ulcer most likely penetrated which of the following arteries?

- ☐ A. Common hepatic
- ☐ B. Gastroduodenal
- ☐ C. Inferior pancreaticoduodenal
- ☐ D. Left gastric
- ☐ E. Right gastroepiploic
- ☐ F. Splenic
- ☐ G. Superior mesenteric



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Feedback



Suspend



End Block



history is significant for chronic obstructive pulmonary disease with multiple exacerbations and lumbar spinal stenosis. The patient has smoked 1 pack of cigarettes daily for 40 years. Blood pressure is 70/40 mm Hg and pulse is 120/min. Examination shows epigastric tenderness. The patient dies an hour after admission despite resuscitation efforts. Autopsy shows a deep peptic ulcer localized proximally on the lesser curvature of the stomach. The ulcer most likely penetrated which of the following arteries?

- ☐ A. Common hepatic (1%)
- ☐ B. Gastroduodenal (9%)
- ☐ C. Inferior pancreaticoduodenal (0%)
- ☒ D. Left gastric (75%)
- ☐ E. Right gastroepiploic (6%)
- ☐ F. Splenic (5%)
- ☐ G. Superior mesenteric (0%)

Correct

75%



20 secs



08/26/2020

Block Time Remaining: 00:30:03

TUTOR

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Feedback

Suspend

End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

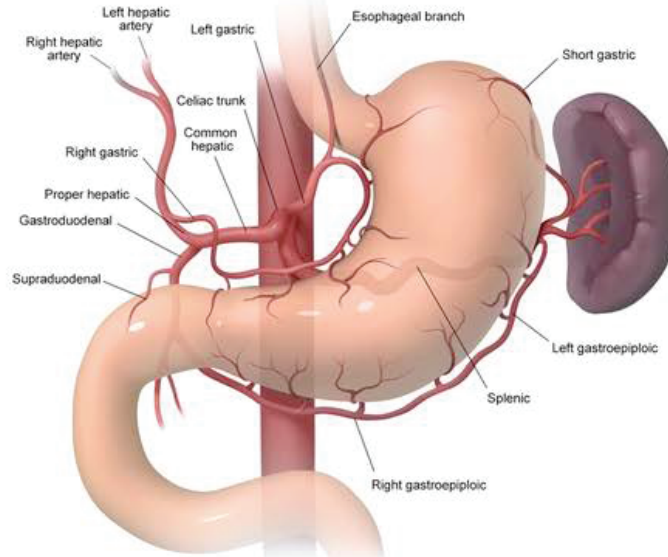
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Text Zoom

Settings

## Exhibit Display

## Upper abdominal vasculature



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Zoom Out

Reset

New | Existing

My Notebook



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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Massive hemorrhage with hypovolemic shock is a potential life-threatening complication of peptic ulcer disease (PUD). Most cases of PUD are due to *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug use. Other risk factors include smoking, glucocorticoid use, and older age.

Most **gastric ulcers** arise along the **lesser curvature** of the stomach, usually at the transitional zone between the gastric corpus (body) and antrum. Glands in the corpus contain parietal cells that produce hydrochloric acid and intrinsic factor; mucosal glands in the antrum contain G cells that secrete gastrin. This **transitional zone** provides the optimal microenvironment (eg, pH, host immune factors) for *H pylori* proliferation. The resultant inflammation leads to mucosal atrophy and ulcer formation.

The left and right **gastric arteries** run along and perfuse the lesser curvature of the stomach, and are a common source of hemorrhage from penetrating gastric ulcers. Other potential complications of PUD include penetration into other adjacent structures (eg, biliary tract, colon), gastric outlet obstruction, and free wall perforation with peritonitis.

**(Choices A and B)** The common hepatic artery perfuses the liver, gallbladder, pylorus, duodenum, and pancreas. It arises from the celiac trunk and ends when it bifurcates into the proper hepatic and gastroduodenal arteries. The gastroduodenal artery supplies blood to the pylorus and proximal duodenum. Ulcers in the posterior duodenal bulb can erode into the gastroduodenal artery, but a gastric



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

free wall perforation with peritonitis.

**(Choices A and B)** The common hepatic artery perfuses the liver, gallbladder, pylorus, duodenum, and pancreas. It arises from the celiac trunk and ends when it bifurcates into the proper hepatic and gastroduodenal arteries. The gastroduodenal artery supplies blood to the pylorus and proximal duodenum. Ulcers in the posterior duodenal bulb can erode into the gastroduodenal artery, but a gastric ulcer at the lesser curvature would not involve these arteries.

**(Choices C and G)** The superior mesenteric and inferior pancreaticoduodenal arteries do not perfuse the stomach.

**(Choice E)** The right gastroepiploic artery arises from the gastroduodenal artery and perfuses the distal greater curvature of the stomach. Gastric ulcers do not commonly occur in the greater curvature.

**(Choice F)** The splenic artery arises from the celiac trunk and supplies blood to the spleen. It is separated from the posterior wall of the stomach by the pancreas and is only rarely penetrated by gastric ulcers.

### Educational objective:

Most gastric ulcers arise along the lesser curvature of the stomach, usually at the transitional zone between the gastric corpus (body) and antrum. The left and right gastric arteries run along the lesser curvature and are likely to be penetrated by ulcers, causing gastric bleeding.



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 3-week-old-girl in the neonatal intensive care unit develops abdominal distension, vomiting, and blood-streaked stools. She had previously tolerated formula feeds and had normal stool and urine output. She was born at 27 weeks gestation to an 18-year-old-mother. The pregnancy was complicated by premature rupture of membranes and preterm delivery. Abdominal x-ray shows thin curvilinear areas of lucency that parallel the bowel wall lumen. Which of the following is the most likely diagnosis?

- ☐ A. Duodenal atresia
- ☐ B. Hirschsprung disease
- ☐ C. Malrotation with volvulus
- ☐ D. Necrotizing enterocolitis
- ☐ E. Pyloric stenosis

**Submit**

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom





Settings

A 3-week-old-girl in the neonatal intensive care unit develops abdominal distension, vomiting, and blood-streaked stools. She had previously tolerated formula feeds and had normal stool and urine output. She was born at 27 weeks gestation to an 18-year-old-mother. The pregnancy was complicated by premature rupture of membranes and preterm delivery. Abdominal x-ray shows thin curvilinear areas of lucency that parallel the bowel wall lumen. Which of the following is the most likely diagnosis?

- ☐ A. Duodenal atresia (3%)
- ☐ B. Hirschsprung disease (6%)
- ☐ C. Malrotation with volvulus (17%)
- ☒ D. Necrotizing enterocolitis (69%)
- ☐ E. Pyloric stenosis (2%)

Correct

 69%  
Answered correctly 01 min, 26 secs  
Time Spent 02/02/2021  
Last Updated

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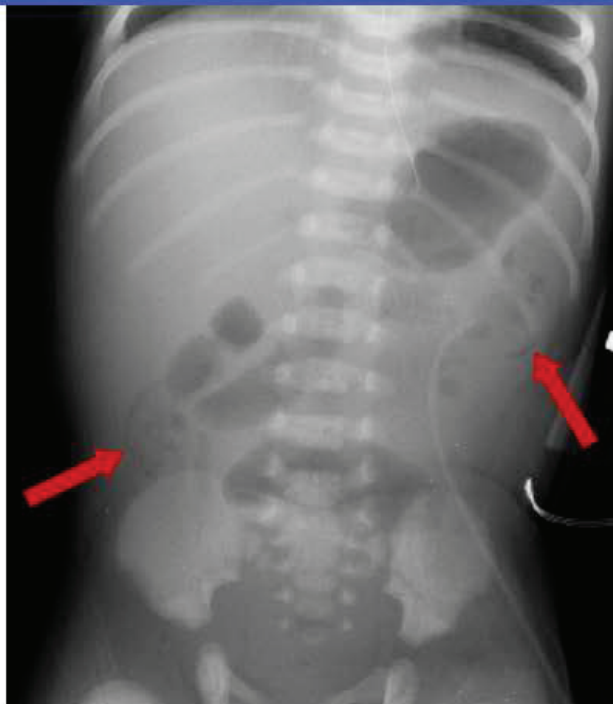


Suspend



End Block

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



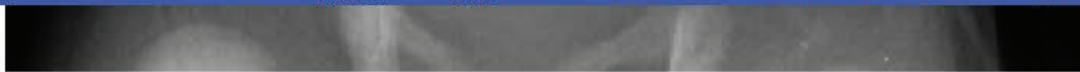
Reverse Color



Text Zoom



Settings



This infant has **pneumatosis intestinalis** (ie, air in the bowel wall), which can be seen on abdominal x-ray as thin curvilinear areas of lucency (red arrows) that parallel the lumen. In an infant with abdominal distension and bloody stools, this finding is diagnostic for **necrotizing enterocolitis** (NEC).

NEC is one of the most frequent gastrointestinal emergencies affecting newborns. It occurs predominantly in **preterm infants** secondary to gastrointestinal and immunologic immaturity. Upon initiation of enteral feeding, bacteria are introduced into the bowel where they proliferate excessively due to compromised immune clearance. Impaired mucosal barrier function allows the bacteria to invade the bowel wall, causing inflammation and **ischemic necrosis** of the terminal ileum and colon. As the disease progresses, the bowel becomes congested and gangrenous with the formation of **intramural gas collections**.

Up to 30% of affected neonates die, especially when disease is complicated by intestinal perforation. Survivors are at risk for strictures and **bowel obstruction** secondary to fibrosis that occurs as the inflammation subsides.

**(Choice A)** Duodenal atresia classically presents with the **double bubble sign** of air in the stomach and proximal duodenal pouch. Affected infants generally have bilious emesis shortly after birth.



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Feedback



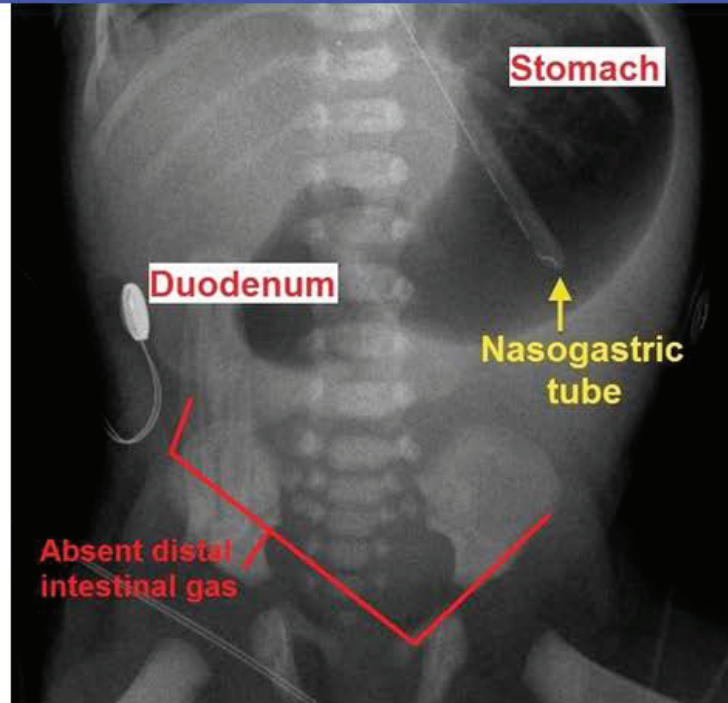
Suspend



End Block



Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice B)** Hirschsprung disease manifests with failure to pass meconium in the first 48 hours after birth. On x-ray, the large intestine appears dilated proximal to the aganglionic portion of bowel; contrast enema will show a narrow-caliber **transition zone**.

**(Choice C)** Malrotation of the bowel occurs when the midgut does not rotate normally during the first trimester, leaving the small and large bowel malpositioned. Malrotated bowel is at high risk of obstruction and ischemia due to twisting around its blood supply (volvulus). However, the finding of pneumatosis intestinalis is more specific for necrotizing enterocolitis.

**(Choice E)** Pyloric stenosis is caused by hypertrophy of the pyloric sphincter and leads to gastric outlet obstruction. It presents with nonbilious vomiting after feeding and a palpable ball of muscle ("olive") in the abdomen. Pyloric stenosis is not associated with bloody stools or pneumatosis intestinalis.

### Educational objective:

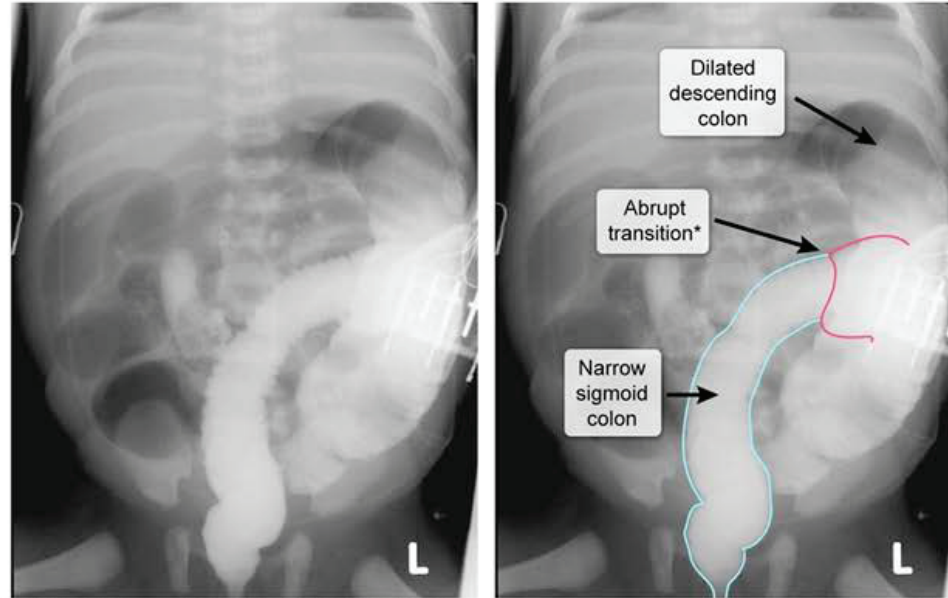
Necrotizing enterocolitis is one of the most common gastrointestinal emergencies affecting newborns. It is characterized by bacterial invasion and ischemic necrosis of the bowel wall, and is associated with prematurity and initiation of enteral feeding. Abdominal x-ray showing pneumatosis intestinalis (ie, air in the bowel wall) confirms the diagnosis.

### References



### Exhibit Display

## Hirschsprung disease



\*Between narrow, aganglionic colon and dilated proximal colon

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Zoom In

Zoom Out

Reset

New | Existing

My Notebook

### References





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 26-year-old woman is evaluated for intermittent abdominal pain occurring over the last several years. The pain is crampy without radiation and graded 6/10 in intensity. She also has fluctuating diarrhea but has not seen blood in the stool. The patient has no nausea, vomiting, constipation, urinary frequency, dysuria, or vaginal symptoms. Her last menstrual period was 2 weeks ago. She does not use tobacco or alcohol. Temperature is 37.2 C (99 F), blood pressure is 115/70 mm Hg, and pulse is 90/min. On examination, the abdomen is tender without guarding or rebound. There is a draining fistula near her coccyx. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Crohn disease
- ☐ B. Diverticulitis
- ☐ C. Intergluteal pilonidal disease
- ☐ D. Irritable bowel syndrome
- ☐ E. Ulcerative colitis

**Submit**

Block Time Remaining: 00:31:30

TUTOR

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0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 26-year-old woman is evaluated for intermittent abdominal pain occurring over the last several years. The pain is crampy without radiation and graded 6/10 in intensity. She also has fluctuating diarrhea but has not seen blood in the stool. The patient has no nausea, vomiting, constipation, urinary frequency, dysuria, or vaginal symptoms. Her last menstrual period was 2 weeks ago. She does not use tobacco or alcohol. Temperature is 37.2 C (99 F), blood pressure is 115/70 mm Hg, and pulse is 90/min. On examination, the abdomen is tender without guarding or rebound. There is a draining fistula near her coccyx. Which of the following is the most likely diagnosis in this patient?

- ☒ A. Crohn disease (78%)
- ☐ B. Diverticulitis (4%)
- ☐ C. Intergluteal pilonidal disease (5%)
- ☐ D. Irritable bowel syndrome (6%)
- ☐ E. Ulcerative colitis (4%)



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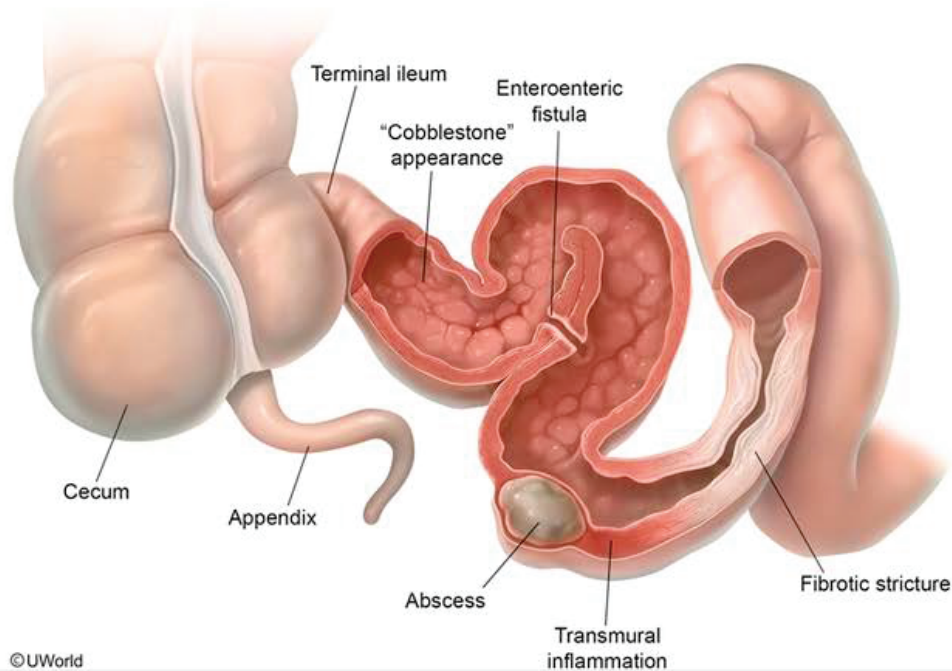
Suspend



End Block

Exhibit Display

# Crohn disease



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

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Inflammation





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



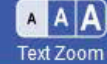
Notes



Calculator



Reverse Color



Text Zoom



Settings

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inflammation

This patient likely has **Crohn disease (CD)** complicated by a perianal fistula. CD can involve the gastrointestinal tract anywhere from the mouth to the anus but often spares the rectum. Patients typically present insidiously (over the course of years) with bouts of crampy abdominal pain, diarrhea, and constitutional symptoms (eg, fatigue, weight loss, fever). Fecal occult blood testing is often positive; however, grossly bloody stool is less commonly seen unless the colon is involved.

Patients are prone to developing fistulas and abscesses due to the **transmural** inflammation that occurs in CD. **Fistulas** are abnormal connections between 2 epithelial-lined organs. They are usually formed between the bowel and nearby structures that include the skin (enterocutaneous), urinary bladder (enterovesical), vagina (enterovaginal), or bowel (enteroenteric). **Perianal disease** other than fistulas is also common and may include [skin tags](#) and fissures.

**(Choice B)** Diverticulitis is characterized by inflammation of saclike protrusions (diverticula) that typically form in the sigmoid colon of older patients. It can present with left lower quadrant abdominal pain, diarrhea or constipation, low-grade fever, and fistulas; however, this patient's young age makes the diagnosis less likely.

**(Choice C)** Intergluteal pilonidal disease is an acquired skin infection involving the upper natal cleft of the



0



Feedback



Suspend



End Block

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

likely.

**(Choice C)** Intergluteal pilonidal disease is an acquired skin infection involving the upper natal cleft of the buttocks. Although patients may present with draining sinus tracts in the intergluteal region, abdominal pain/tenderness and diarrhea are not characteristic.

**(Choice D)** Irritable bowel syndrome (IBS) is characterized by chronic abdominal pain associated with altered bowel habits (eg, diarrhea and/or constipation). Pain is often relieved with bowel movements. IBS is not an inflammatory condition and does not cause fistulas.

**(Choice E)** Ulcerative colitis is an inflammatory disease of the colonic mucosa that almost always affects the rectum and often presents with grossly bloody stool. Fistulas are not commonly seen as inflammation does not involve the full thickness of the bowel wall.

### Educational objective:

Crohn disease typically presents with the insidious onset of abdominal pain, diarrhea, and constitutional symptoms (eg, weight loss, fever). Patients are prone to developing fistulas/abscesses as the lesions affect the entire thickness of the bowel wall. Perianal disease (eg, skin tags, fissures) is also common.

### References

• Diagnosis and management of Crohn's disease



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

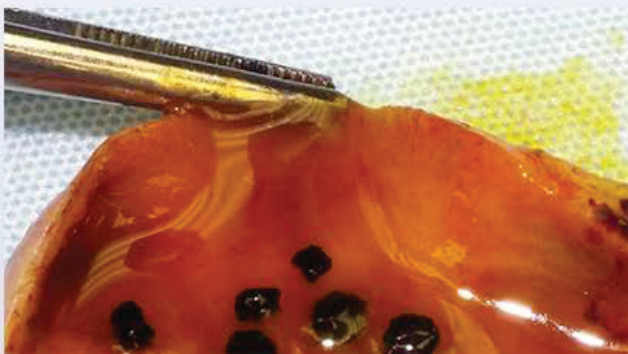


Text Zoom



Settings

A 31-year-old woman comes to the emergency department due to worsening right upper quadrant pain, fever, nausea, and vomiting for a day. The pain increases with deep inspiration. Other medical conditions include uterine fibroids and sickle cell anemia. The patient does not use tobacco, alcohol, or illicit drugs. Temperature is 38.6 C (101.5 F), blood pressure is 120/70 mm Hg, and pulse is 102/min. BMI is 24 kg/m<sup>2</sup>. On examination, the patient appears uncomfortable because of the pain; there is no jaundice. Tenderness and guarding are present over the right upper quadrant. Bowel sounds are decreased. Hemoglobin is 10.1 g/dL and white blood cell count is 18,000/mm<sup>3</sup> with 7% band forms. Abdominal ultrasound shows evidence of cholelithiasis and gallbladder wall thickening. Gross inspection of the specimen obtained during laparoscopic cholecystectomy is shown in the image below:



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Feedback

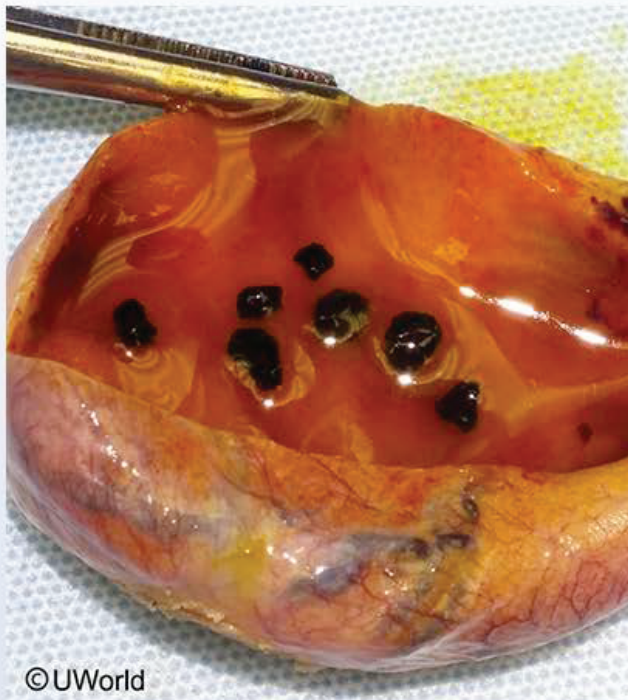


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or cholelithiasis and gallbladder wall thickening. Gross inspection of the specimen obtained during laparoscopic cholecystectomy is shown in the image below:



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Which of the following is most likely responsible for this patient's symptoms?



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



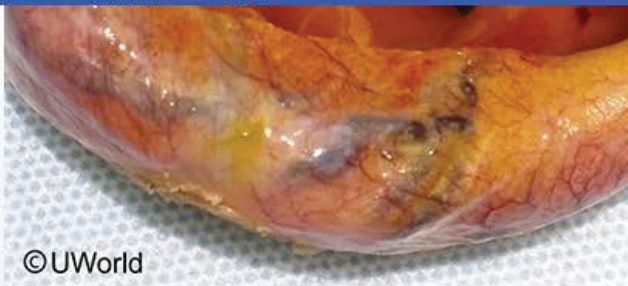
Reverse Color



Text Zoom



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Which of the following is most likely responsible for this patient's symptoms?

- ☐ A. Altered enterohepatic circulation of bilirubin
- ☐ B. Biliary stasis due to lack of enteral stimulation
- ☐ C. Decreased gallbladder motility due to denervation
- ☒ D. Impaired bile acid synthesis
- ☐ E. Increased cholesterol synthesis
- ☐ F. Increased efflux of bilirubin into bile

Submit

Block Time Remaining: 00:32:12

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Feedback



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End Block





Which of the following is most likely responsible for this patient's symptoms?

- ☐ A. Altered enterohepatic circulation of bilirubin (14%)
- ☐ B. Biliary stasis due to lack of enteral stimulation (5%)
- ☐ C. ~~Decreased gallbladder motility due to denervation (2%)~~
- ☐ D. ~~Impaired bile acid synthesis (5%)~~
- ☐ E. ~~Increased cholesterol synthesis (3%)~~
- ☒ F. Increased efflux of bilirubin into bile (68%)

Correct

68%  
Answered correctly

01 min, 19 secs  
Time Spent

12/03/2020  
Last Updated

Block Time Remaining: 00:33:22  
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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



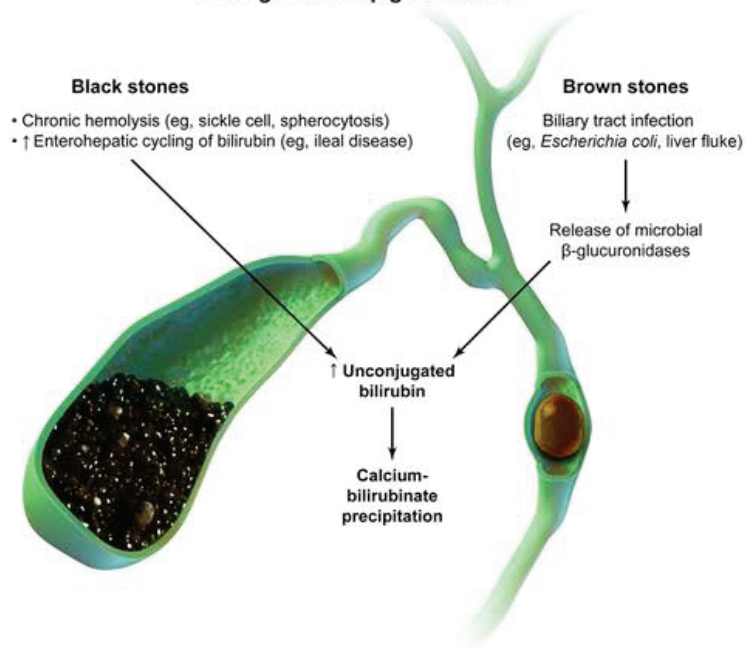
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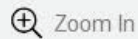
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## Exhibit Display

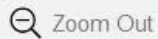
## Pathogenesis of pigment stones



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bilirubinate



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Feedback



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End Block



This patient with fever, right upper quadrant pain, and leukocytosis has **acute cholecystitis**. Cholecystitis is inflammation of the gallbladder that usually occurs when gallstones obstruct the cystic duct. Gallstones form due to supersaturation of bile constituents (eg, cholesterol, bilirubin), which then crystalize out of solution with other bile components (eg, mucin, calcium, proteins) to produce stones.

**Black gallstones**, as seen in this patient, form due to the **supersaturation of bilirubin**, which precipitates with calcium to form multiple small calcium bilirubinate stones. Bilirubin supersaturation occurs through the following mechanisms:

- **Increased bilirubin production:** Chronic hemolysis, as seen in **sickle cell anemia**, hereditary spherocytosis, and thalassemia, increases circulating levels of free bilirubin, which is taken up by the liver and **excreted into bile**.
- **Altered enterohepatic circulation** of bilirubin: Ileal disease (eg, Crohn disease) or resection allows bile acids, which are normally reabsorbed in the ileum, to spill into the colon. There, bile acids solubilize unconjugated bilirubin, allowing its reabsorption and concentration within the bile (**Choice A**).

This patient with sickle cell anemia most likely has chronic hemolysis, which has increased bilirubin efflux into the bile, promoting formation of black stones.







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



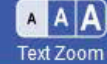
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Reverse Color



Text Zoom



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This patient with sickle cell anemia most likely has chronic hemolysis, which has increased bilirubin efflux into the bile, promoting formation of black stones.

**(Choices B and C)** Biliary stasis promotes gallstone formation by providing a favorable environment for crystal nucleation and aggregation. Stasis can occur due to gallbladder denervation (eg, transection of the nerves that control gallbladder contraction) or decreased stimulation by enterocytes during prolonged fasting (cholecystokinin is released in response to food). However, stasis usually promotes the formation of yellow cholesterol stones, and this patient did not have prolonged fasting or surgery prior to developing her symptoms.

**(Choice D)** Cirrhosis can also occasionally promote the formation of black stones due to impaired bile acid synthesis and hyperbilirubinemia (due to cholestasis). However, this patient does not have a history of cirrhosis or stigmata of chronic liver disease (eg, jaundice).

**(Choice E)** Increased cholesterol synthesis results in the formation of yellow cholesterol gallstones. This typically occurs in the setting of obesity, diabetes mellitus, or certain medications (eg, estrogen-containing oral contraceptives).

**Educational objective:**



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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crystal nucleation and aggregation. Stasis can occur due to gallbladder denervation (eg, transection of the nerves that control gallbladder contraction) or decreased stimulation by enterocytes during prolonged fasting (cholecystokinin is released in response to food). However, stasis usually promotes the formation of yellow cholesterol stones, and this patient did not have prolonged fasting or surgery prior to developing her symptoms.

**(Choice D)** Cirrhosis can also occasionally promote the formation of black stones due to impaired bile acid synthesis and hyperbilirubinemia (due to cholestasis). However, this patient does not have a history of cirrhosis or stigmata of chronic liver disease (eg, jaundice).

**(Choice E)** Increased cholesterol synthesis results in the formation of yellow cholesterol gallstones. This typically occurs in the setting of obesity, diabetes mellitus, or certain medications (eg, estrogen-containing oral contraceptives).

### Educational objective:

Black gallstones form due to supersaturation of the bile with bilirubin, which precipitates with calcium to form calcium bilirubinate stones. This typically occurs in the setting of chronic hemolysis (eg, sickle cell disease) or altered enterohepatic circulation of bilirubin (eg, Crohn disease, ileal resection).

### References



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Researchers studying gastrointestinal pathophysiology analyze hundreds of gastric mucosal biopsy specimens taken from patients who underwent endoscopy at a local tertiary care center. They notice that colonization of the gastric antrum with S-shaped, gram-negative bacteria is associated with a decreased number of somatostatin-producing antral cells. Depletion of these cells from the gastric antrum is most likely to cause which of the following conditions?

- ☐ A. Chronic pancreatitis
- ☐ B. Duodenal ulcers
- ☐ C. Gastric lymphoma
- ☐ D. Gastric ulcers
- ☐ E. Vitamin B<sub>12</sub> deficiency

**Submit**

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom




Settings

Researchers studying gastrointestinal pathophysiology analyze hundreds of gastric mucosal biopsy specimens taken from patients who underwent endoscopy at a local tertiary care center. They notice that colonization of the gastric antrum with S-shaped, gram-negative bacteria is associated with a decreased number of somatostatin-producing antral cells. Depletion of these cells from the gastric antrum is most likely to cause which of the following conditions?

- ☐ A. Chronic pancreatitis (1%)
- ☒ B. Duodenal ulcers (62%)
- ☐ C. Gastric lymphoma (2%)
- ☐ D. Gastric ulcers (30%)
- ☐ E. Vitamin B<sub>12</sub> deficiency (2%)

Correct

 62%  
Answered correctly 01 min, 28 secs  
Time Spent 09/18/2020  
Last Updated

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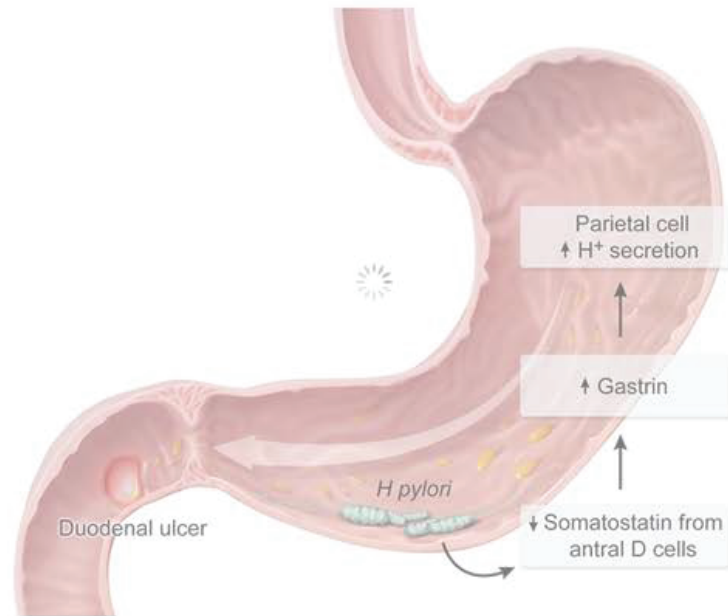
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*Helicobacter pylori* and duodenal ulcers



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New | Existing

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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***Helicobacter pylori*** is a motile, spiral-shaped, gram-negative bacteria found attached to the gastric mucosa or deep in the mucus layer overlying the gastric epithelium. It is protected from gastric acid by endogenous urease production: **urease** converts urea to ammonia, which alkalinizes the surrounding pH but injures gastric epithelial cells. Damage to the gastric mucosa is compounded by localized inflammation due to the immunologic response against *H pylori*.

Chronic inflammation due to *H pylori* colonization in the **gastric antrum** leads to **depletion of somatostatin-producing cells** (delta cells), which are located mostly in the antrum. Somatostatin inhibits gastrin release from G-cells. In its absence, **elevated gastrin** levels act directly (via cholecystokinin B receptors) and indirectly (via histamine release by enterochromaffin-like cells) to **increase acid secretion** by parietal cells. In addition, *H pylori* releases cytotoxins that inhibit duodenal production of bicarbonate. The resultant increased acid load is emptied into the under-protected duodenum, leading to **duodenal ulcer** formation.

In contrast, gastric ulcers occur when *H pylori* colonizes the gastric body (corpus) (**Choice D**). Chronic inflammation leads to multifocal atrophic gastritis and a reduction in the number of acid-producing **parietal cells**, which are located mostly in the gastric body. Delta cells in the antrum are not markedly reduced,



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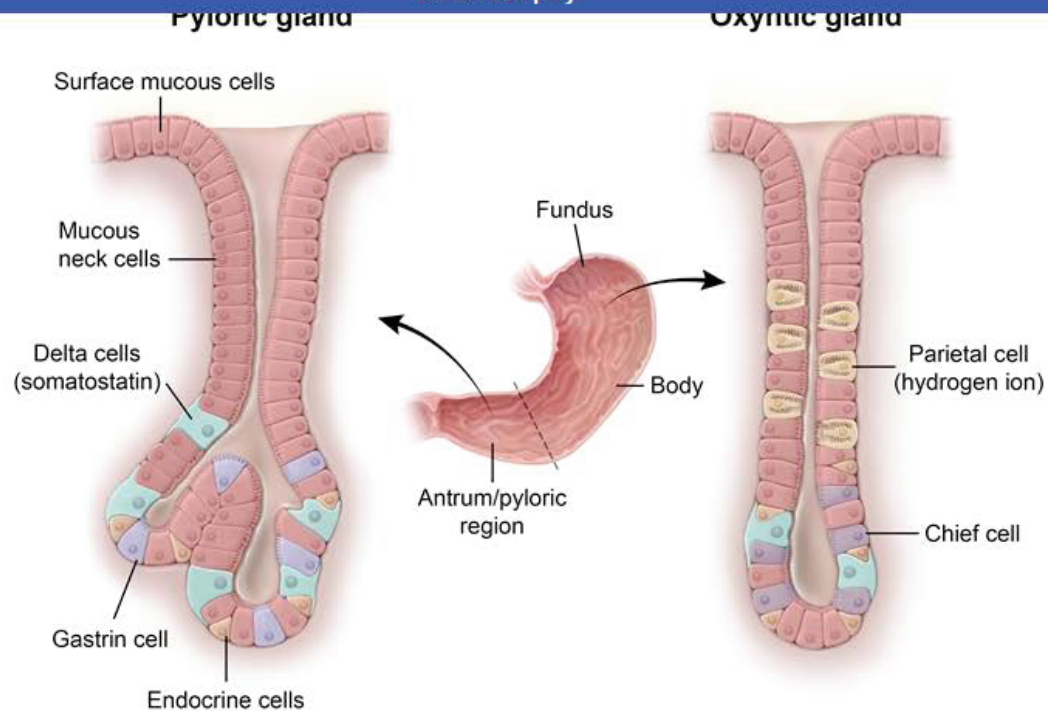
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End Block



Exhibit Display



Zoom In Zoom Out Reset New Existing My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

In contrast, gastric ulcers occur when *H pylori* colonizes the gastric body (corpus) (**Choice D**). Chronic inflammation leads to multifocal atrophic gastritis and a reduction in the number of acid-producing parietal cells, which are located mostly in the gastric body. Delta cells in the antrum are not markedly reduced, therefore acid secretion is often low to normal. Gastric ulcer formation results from direct mucosal damage caused by bacterial products (eg, ammonia, cytotoxins) and the resultant inflammatory response. Unlike antral-predominant disease, corpus-predominant disease is associated with metaplasia and malignancies (eg, gastric lymphoma, adenocarcinoma) (**Choice C**).

(**Choice A**) Chronic pancreatitis is not associated with *H pylori* infection. It is most frequently caused by chronic alcoholism or obstruction of the pancreatic ducts due to gallstones or malignancy.

(**Choice E**) Vitamin B<sub>12</sub> deficiency can result from autoimmune gastritis. Autoimmune gastritis is characterized by autoantibodies against gastric parietal cells leading to inflammation of the gastric mucosa, parietal cell destruction, and achlorhydria. Its etiology is at least partially genetic.

### Educational objective:

*Helicobacter pylori* antral gastritis is associated with the formation of duodenal ulcers due to increased gastric acid production. This increase in acidity is caused by unchecked gastrin production due to the destruction of somatostatin-secreting cells in the gastric antrum.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 35-year-old woman comes to the clinic due to severe heartburn that is resistant to over-the-counter antacids. The patient has no known medical problems and takes no other medications. She occasionally has a glass of wine with dinner but does not use tobacco or illicit drugs. Physical examination shows scattered telangiectasias on the face, several ulcers at the tips of the fingers, and small calcium deposits in the soft tissues of the hands and elbows. Which of the following processes is the most likely cause of this patient's heartburn?

- ☐ A. Abnormal location of the gastroesophageal junction
- ☐ B. Fibrous replacement of the muscularis in the lower esophagus
- ☐ C. Increased gastric acid production
- ☐ D. Increase in resting lower esophageal sphincter tone
- ☐ E. Uncoordinated, simultaneous muscle contractions in the lower esophagus

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 35-year-old woman comes to the clinic due to severe heartburn that is resistant to over-the-counter antacids. The patient has no known medical problems and takes no other medications. She occasionally has a glass of wine with dinner but does not use tobacco or illicit drugs. Physical examination shows scattered telangiectasias on the face, several ulcers at the tips of the fingers, and small calcium deposits in the soft tissues of the hands and elbows. Which of the following processes is the most likely cause of this patient's heartburn?

- ☐ A. Abnormal location of the gastroesophageal junction (3%)
- ☒ B. Fibrous replacement of the muscularis in the lower esophagus (55%)
- ☐ C. Increased gastric acid production (16%)
- ☐ D. Increase in resting lower esophageal sphincter tone (6%)
- ☐ E. Uncoordinated, simultaneous muscle contractions in the lower esophagus (17%)

Correct

 55%  
Answered correctly 01 min, 44 secs  
Time Spent 02/08/2021  
Last Updated

Block Time Remaining: 00:36:34

TUTOR

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient has features consistent with **CREST syndrome** (ie, **Calcinosis**, **Raynaud** phenomenon, **Esophageal** dysmotility, **Sclerodactyly**, **Telangiectasia**), a limited variant of systemic sclerosis with skin disease that primarily affects the face, forearms, and fingers. The pathogenesis of systemic sclerosis involves chronic autoimmune inflammation, vascular endothelial injury resulting in chronic ischemic tissue damage (eg, **fingertip ulcers**), and excessive activation of fibroblasts leading to progressive tissue fibrosis.

Esophageal dysmotility is a result of **atrophy** and **fibrous replacement** of the muscularis in the lower esophagus. The esophageal body and the lower esophageal sphincter become atonic and dilated, resulting in symptoms of **gastroesophageal reflux** (eg, heartburn, regurgitation, dysphagia). This increases the risk of Barrett's esophagus and fibrous stricture formation.

**(Choice A)** A sliding hiatal hernia is characterized by herniation of the gastroesophageal junction and a portion of the stomach through the esophageal hiatus, which predisposes patients to gastroesophageal reflux.

**(Choice C)** Increased gastric acid production occurs with gastrinomas, gastrin-secreting neuroendocrine tumors of the small intestine/pancreas that often present with multiple or medically refractory peptic ulcers.

**(Choice D)** Achalasia is an esophageal motility disorder characterized by failed relaxation of the lower esophageal sphincter resulting in food retention, dilation of the esophageal body, and symptoms of





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient has features consistent with CREST syndrome (ie, Calcinosis, Raynaud phenomenon,

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

tumors of the small intestine/pancreas that often present with multiple or medically refractory peptic ulcers.

**(Choice D)** Achalasia is an esophageal motility disorder characterized by failed relaxation of the lower esophageal sphincter resulting in food retention, dilation of the esophageal body, and symptoms of solid/liquid dysphagia.

**(Choice E)** Diffuse esophageal spasm is characterized by periodic, uncoordinated, simultaneous contractions of the lower esophagus due to impaired inhibitory innervation within the esophageal myenteric plexus. Patients typically have liquid/solid dysphagia and chest pain due to inefficient propagation of food into the stomach.

### Educational objective:

Systemic sclerosis may result in esophageal dysmotility and incompetence of the lower esophageal sphincter due to atrophy and fibrous replacement of the esophageal muscularis. This can cause gastroesophageal reflux with an increased risk of Barrett's esophagus and stricture formation.

### References

- [Diagnosis and classification of systemic sclerosis.](#)
- [Diagnosis and treatment of scleroderma.](#)



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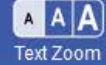
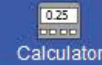
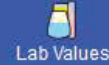
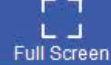
Feedback



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A pharmaceutical researcher is trying to develop a vaccine against the hepatitis C virus. She infects a chimpanzee with hepatitis C virus of known genotype and subtype. Several weeks later, a liver sample is obtained, and viral RNAs are extracted from the hepatocytes. A genetic study of the viral genomes reveals that the extracted RNA sequences vary significantly from that of the original infecting virus. This genetic instability is most likely due to the lack of which of the following features during the viral replication process?

- ☐ A. 3' → 5' exonuclease activity
- ☐ B. 5' → 3' exonuclease activity
- ☐ C. Glycosylase activity
- ☐ D. Ligase activity
- ☐ E. Nucleotide specificity
- ☐ F. Primase activity

**Submit**

Block Time Remaining: 00:36:35

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Feedback

Suspend

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Previous



Next



Full Screen



Tutorial



Lab Values



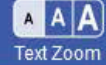
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Calculator



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Settings

A pharmaceutical researcher is trying to develop a vaccine against the hepatitis C virus. She infects a chimpanzee with hepatitis C virus of known genotype and subtype. Several weeks later, a liver sample is obtained, and viral RNAs are extracted from the hepatocytes. A genetic study of the viral genomes reveals that the extracted RNA sequences vary significantly from that of the original infecting virus. This genetic instability is most likely due to the lack of which of the following features during the viral replication process?

- ☒ A. 3' → 5' exonuclease activity (67%)
- ☐ B. 5' → 3' exonuclease activity (20%)
- ☐ C. Glycosylase activity (2%)
- ☐ D. Ligase activity (2%)
- ☐ E. Nucleotide specificity (5%)
- ☐ F. Primase activity (2%)



1



Feedback



Suspend



End Block





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**Hepatitis C virus (HCV)** has  $\geq 6$  genotypes and multiple subgenotypes. These variant strains differ primarily at **hypervariable** genomic regions, such as those found in the sequences encoding its 2 **envelope glycoproteins**. Moreover, there is **no proofreading 3' → 5'** exonuclease activity built into the virion-encoded RNA polymerase. As a result, the RNA polymerase makes many errors during replication, and several dozen subspecies of HCV are typically present in the blood of an infected individual at any one time.

**(Choice B)** 5' → 3' exonuclease activity allows DNA polymerase I to engage in nick translation, which is important for both DNA repair and removal of RNA primers during replication. This feature is not the cause of instability in HCV.

**(Choice C)** DNA glycosylase is important in base excision repair as it removes the nitrogen base from the sugar-phosphate backbone. An endonuclease then completes the remainder of the repair. This enzyme is not the cause of instability in HCV.

**(Choice D)** DNA ligase is used to join 2 fragments of DNA and is therefore necessary for both DNA repair and replication. The HCV genome is a single-stranded, positive-sense RNA molecule that does not require ligase activity during replication.



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Feedback



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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



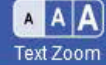
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**(Choice C)** DNA glycosylase is important in base excision repair as it removes the nitrogen base from the sugar-phosphate backbone. An endonuclease then completes the remainder of the repair. This enzyme is not the cause of instability in HCV.

**(Choice D)** DNA ligase is used to join 2 fragments of DNA and is therefore necessary for both DNA repair and replication. The HCV genome is a single-stranded, positive-sense RNA molecule that does not require ligase activity during replication.

**(Choice E)** Nucleotide specificity refers to the importance of inserting the correct nucleotide (eg, adenine, guanine, cytosine, thymine, uracil) into a strand of DNA or RNA. It is not the cause of instability in HCV.

**(Choice F)** DNA primase is a form of RNA polymerase. In bacteria, it binds with DNA helicase and synthesizes a short RNA primer to which nucleotides can be added by DNA polymerase. This enzyme is not the cause of instability in HCV.

### Educational objective:

The hepatitis C virus is genetically unstable because it lacks proofreading 3' → 5' exonuclease activity in its RNA polymerase. Its envelope glycoprotein sequences also contain a hypervariable region prone to frequent genetic mutation.



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Feedback



Suspend



End Block



A 31-year-old previously healthy man comes to the office due to myalgias, anorexia, and skin rash. He does not use tobacco, alcohol, or illicit drugs. The patient works as a personal trainer and is a bodybuilding enthusiast. He denies using anabolic steroids but has been consuming large amounts of raw egg whites for the past several months. Physical examination shows macular dermatitis of the extremities. A water-soluble vitamin deficiency is suspected as the cause of his condition. Which of the following biochemical conversions most likely uses the deficient vitamin as a cofactor?

- ☐ A. Glucose to ribose-5-phosphate
- ☐ B. Pyruvate to acetyl-CoA
- ☐ C. Pyruvate to alanine
- ☐ D. Pyruvate to oxaloacetate
- ☐ E. Succinate to oxaloacetate

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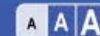




A 31-year-old previously healthy man comes to the office due to myalgias, anorexia, and skin rash. He does not use tobacco, alcohol, or illicit drugs. The patient works as a personal trainer and is a bodybuilding enthusiast. He denies using anabolic steroids but has been consuming large amounts of raw egg whites for the past several months. Physical examination shows macular dermatitis of the extremities. A water-soluble vitamin deficiency is suspected as the cause of his condition. Which of the following biochemical conversions most likely uses the deficient vitamin as a cofactor?

- ☐ A. Glucose to ribose-5-phosphate
- ☐ B. Pyruvate to acetyl-CoA
- ☐ C. Pyruvate to alanine
- ☒ D. Pyruvate to oxaloacetate
- ☐ E. Succinate to oxaloacetate

**Submit**



A 31-year-old previously healthy man comes to the office due to myalgias, anorexia, and skin rash. He does not use tobacco, alcohol, or illicit drugs. The patient works as a personal trainer and is a bodybuilding enthusiast. He denies using anabolic steroids but has been consuming large amounts of raw egg whites for the past several months. Physical examination shows macular dermatitis of the extremities. A water-soluble vitamin deficiency is suspected as the cause of his condition. Which of the following biochemical conversions most likely uses the deficient vitamin as a cofactor?

- ☐ A. Glucose to ribose-5-phosphate (6%)
- ☐ B. Pyruvate to acetyl-CoA (24%)
- ☐ C. Pyruvate to alanine (8%)
- ☒ D. Pyruvate to oxaloacetate (50%)
- ☐ E. Succinate to oxaloacetate (9%)

Correct

50%  
Answered correctly01 min, 27 secs  
Time Spent09/28/2020  
Last Updated

Block Time Remaining: 00:01:28

TUTOR

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**Biotin (vitamin B<sub>7</sub>) as a cofactor**

Enzyme	Reaction
Pyruvate carboxylase	Pyruvate to oxaloacetate (gluconeogenesis)
Acetyl-CoA carboxylase	Acetyl-CoA to malonyl-CoA (fatty acid synthesis)
Propionyl-CoA carboxylase	Propionyl-CoA to methylmalonyl-CoA (fatty acid oxidation)

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**Biotin (vitamin B<sub>7</sub>)** is an important cofactor for several **carboxylase** enzymes. It functions as a CO<sub>2</sub> carrier and plays an essential role in carbohydrate, lipid, and amino acid metabolism. In the liver, the conversion of **pyruvate to oxaloacetate** for gluconeogenesis requires pyruvate carboxylase and biotin.

Biotin deficiency is rare but can occur secondary to poor diet, excessive raw egg white consumption (due to high levels of **biotin-binding avidin** in egg whites), and congenital disorders of biotin metabolism. Patients with biotin deficiency present with nonspecific symptoms, including changes in mental status, myalgias, anorexia, and chronic **dermatologic changes** such as macular dermatitis. Biotin-deficient individuals can



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Feedback



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high levels of **biotin-binding avidin** in egg whites), and congenital disorders of biotin metabolism. Patients with biotin deficiency present with nonspecific symptoms, including changes in mental status, myalgias, anorexia, and chronic **dermatologic changes** such as macular dermatitis. Biotin-deficient individuals can also develop **metabolic acidosis** as a result of increased conversion of pyruvate to lactic acid.

**(Choice A)** Niacin (vitamin B<sub>3</sub>), in the form of NADP<sup>+</sup>, is used to oxidize glucose-6-phosphate in the pentose phosphate pathway, generating ribose-5-phosphate and NADPH in the process.

**(Choice B)** Thiamine (vitamin B<sub>1</sub>), riboflavin (vitamin B<sub>2</sub>), niacin (vitamin B<sub>3</sub>), pantothenic acid (vitamin B<sub>5</sub>), and lipoic acid are the 5 cofactors required by the mitochondrial enzyme complex **pyruvate dehydrogenase**. In their absence, the metabolism of pyruvate to acetyl-CoA is not possible.

**(Choice C)** Pyridoxal phosphate (vitamin B<sub>6</sub>) acts as a cofactor for **alanine transaminase**, which catalyzes the reversible reaction between pyruvate and glutamate to alanine and alpha-ketoglutarate in the liver and muscle tissue.

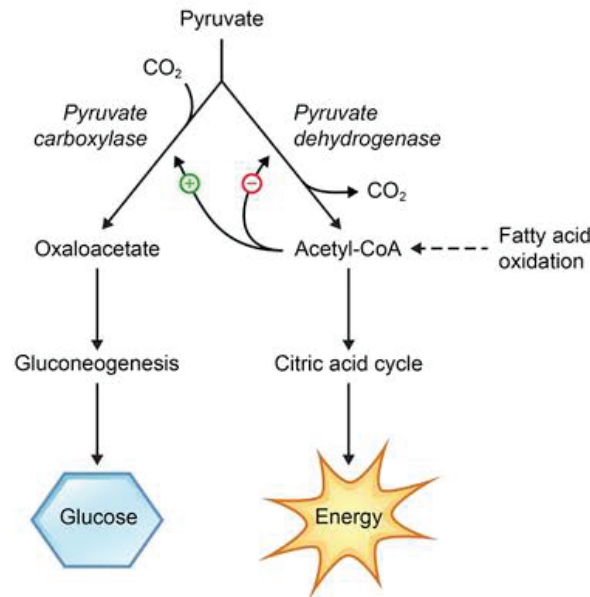
**(Choice E)** Production of oxaloacetate from succinate in the TCA cycle requires 2 enzymes (succinate dehydrogenase and malate dehydrogenase), along with riboflavin (vitamin B<sub>2</sub>) and niacin (vitamin B<sub>3</sub>) in the forms of cofactors FAD<sup>+</sup> and NAD<sup>+</sup>, respectively.



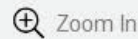
high levels of biotin-binding avidin in egg whites) and congenital disorders of biotin metabolism. Patients

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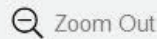
## Metabolic fate of pyruvate



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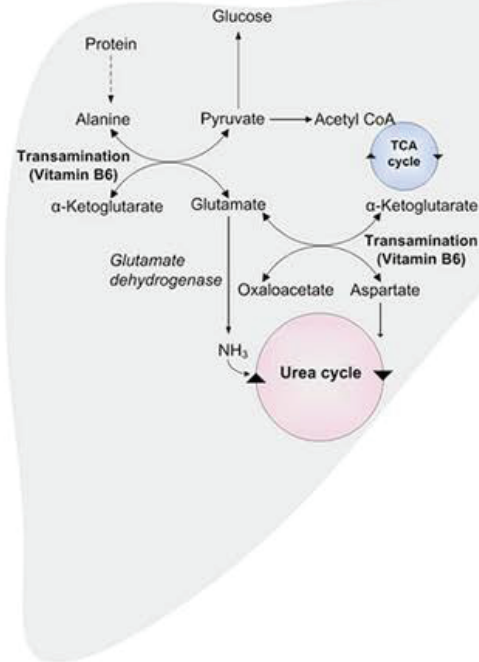
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high levels of biotin-binding avidin in egg whites) and congenital disorders of biotin metabolism. Patients

## Exhibit Display



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and lipids are the cofactors required by the mitochondrial enzyme complex **pyruvate dehydrogenase**. In their absence, the metabolism of pyruvate to acetyl-CoA is not possible.

**(Choice C)** Pyridoxal phosphate (vitamin B<sub>6</sub>) acts as a cofactor for **alanine transaminase**, which catalyzes the reversible reaction between pyruvate and glutamate to alanine and alpha-ketoglutarate in the liver and muscle tissue.

**(Choice E)** Production of oxaloacetate from succinate in the TCA cycle requires 2 enzymes (succinate dehydrogenase and malate dehydrogenase), along with riboflavin (vitamin B<sub>2</sub>) and niacin (vitamin B<sub>3</sub>) in the forms of cofactors FAD<sup>+</sup> and NAD<sup>+</sup>, respectively.

### Educational objective:

Biotin acts as a CO<sub>2</sub> carrier on the surface of carboxylase enzymes and is an essential cofactor for numerous reactions, including the conversion of pyruvate to oxaloacetate and fatty acid metabolism.

Excess ingestion of avidin, found in egg whites, has been associated with biotin deficiency. This condition presents with mental status changes, myalgias, anorexia, macular dermatitis, and lactic acidosis.

Biochemistry

Gastrointestinal & Nutrition

Tca cycle

Subject

System

Topic

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A 62-year-old man comes to the office due to watery diarrhea. He has also been having episodes of dyspnea and wheezing. His wife has noticed that he sometimes becomes very flushed and red. The patient has no abdominal pain, vomiting, cough, or fever. He has a history of hypertension and takes amlodipine. He does not use tobacco, alcohol, or illicit drugs. His blood pressure is 140/70 mm Hg and pulse is 82/min. Cardiopulmonary examination is unremarkable. The abdomen is soft and nontender. Chest x-ray is normal, and the abdominal CT scan reveals mass lesions in the right liver lobe and ileum. Surgery is scheduled to resect the tumors. Which of the following medications can be used to relieve this patient's symptoms prior to surgery?

- ☐ A. Cabergoline
- ☐ B. Leuprolide
- ☐ C. Octreotide
- ☐ D. Phenoxybenzamine
- ☐ E. Rituximab





dyspnea and wheezing. His wife has noticed that he sometimes becomes very flushed and red. The patient has no abdominal pain, vomiting, cough, or fever. He has a history of hypertension and takes amlodipine. He does not use tobacco, alcohol, or illicit drugs. His blood pressure is 140/70 mm Hg and pulse is 82/min. Cardiopulmonary examination is unremarkable. The abdomen is soft and nontender. Chest x-ray is normal, and the abdominal CT scan reveals mass lesions in the right liver lobe and ileum. Surgery is scheduled to resect the tumors. Which of the following medications can be used to relieve this patient's symptoms prior to surgery?

- ☐ A. Cabergoline (4%)
- ☐ B. Leuprolide (5%)
- ☒ C. Octreotide (75%)
- ☐ D. Phenoxybenzamine (12%)
- ☐ E. Rituximab (2%)

Correct

75%



44 secs



11/29/2020

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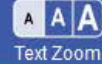
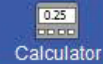
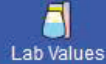
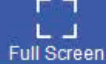


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### Features of carcinoid syndrome

<b>Clinical manifestations</b>	<ul style="list-style-type: none"><li>• Skin: <b>Flushing</b>, telangiectasias, cyanosis</li><li>• Gastrointestinal: <b>Watery diarrhea</b>, cramping</li><li>• Pulmonary: <b>Bronchospasm</b>, dyspnea, wheezing</li><li>• Cardiac: Valvular fibrous plaques (right &gt; left)</li></ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"><li>• Elevated 24-hour urinary excretion of <b>5-HIAA</b></li><li>• CT/MRI of abdomen &amp; pelvis to localize tumor</li></ul>
<b>Treatment</b>	<ul style="list-style-type: none"><li>• Octreotide for symptomatic patients</li><li>• Surgery for liver metastases</li></ul>

5-HIAA = 5-hydroxyindoleacetic acid.

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The combination of wheezing, diarrhea, and facial flushing in association with an ileal tumor with hepatic metastasis is suggestive of **carcinoid syndrome**. Carcinoid tumors (most common ileal tumors) secrete a number of biologically active substances including serotonin and can cause symptoms when they metastasize. Common manifestations of carcinoid syndrome include flushing, asthma-like symptoms (wheezing, dyspnea), diarrhea, and syncope (due to low blood pressure). Long-standing carcinoid





syndrome can cause right-sided valvular heart disease.

The most definitive treatment for carcinoid syndrome is surgical excision. Medical therapy with octreotide can be used to control symptoms. **Octreotide** is a synthetic analog of somatostatin with a longer half-life. It acts on somatostatin receptors and inhibits secretion of many hormones and hormone-like substances. Octreotide is also used to inhibit secretory diarrhea in VIPomas (pancreatic endocrine tumors).

**(Choice A)** Cabergoline is a dopamine agonist used in growth hormone-secreting pituitary tumors or prolactinoma.

**(Choice B)** Leuprolide is a synthetic analog of gonadotropin-releasing hormone (GnRH). Continuous administration suppresses release of LH and FSH. Leuprolide is used in management of prostatic cancer, precocious puberty, and endometriosis.

**(Choice D)** Phenoxybenzamine is an alpha blocker that is used in treatment of pheochromocytoma.

**(Choice E)** Rituximab is a CD20 monoclonal antibody used to treat multiple myeloma, leukemia, and multiple autoimmune disorders.

### Educational objective:

Carcinoid syndrome may accompany extraintestinal metastases of gastrointestinal carcinoid tumors.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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### Educational objective:

Carcinoid syndrome may accompany extraintestinal metastases of gastrointestinal carcinoid tumors.

Octreotide is a synthetic somatostatin analog used to control the symptoms of carcinoid syndrome.

### References

- [Small bowel cancer in the United States: changes in epidemiology, treatment, and survival over the last 20 years.](https://pubmed.ncbi.nlm.nih.gov/19106677/)





A 32-year-old man comes to the office due to fever, jaundice, vomiting, and decreased appetite for the past 5 days. He recently returned home from South America and reports that a couple of his travel companions have had similar symptoms. The patient does not use alcohol, tobacco, or illicit drugs and has no relevant family history. Temperature is 38.8 C (101.8 F), blood pressure is 125/80 mm Hg, pulse is 85/min. Scleral icterus and hepatomegaly are present. Laboratory results are as follows:

#### Complete blood count

Hemoglobin	14.9 g/dL
Platelets	389,000/mm <sup>3</sup>
Leukocytes	15,000/mm <sup>3</sup>

#### Liver function studies

Total bilirubin	3.9 mg/dL
Alkaline phosphatase	185 U/L
Aspartate aminotransferase (SGOT)	2,410 U/L



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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## Liver function studies

Total bilirubin 3.9 mg/dL

Alkaline phosphatase 185 U/L

Aspartate aminotransferase (SGOT) 2,410 U/L

Alanine aminotransferase (SGPT) 3,500 U/L

Which of the following pathophysiologic events is most likely occurring in this patient?

- ☐ A. Activation of hepatic stellate cells
- ☐ B. CD8<sup>+</sup> T-cell response against affected hepatocytes
- ☐ C. Hepatocyte production of a misfolded protein
- ☐ D. Neutrophilic infiltration of the liver
- ☐ E. Plasma cell hepatic migration

Submit

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2



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Mark

Previous

Next



Full Screen



Tutorial



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Notes



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## Liver function studies

Total bilirubin	3.9 mg/dL
Alkaline phosphatase	185 U/L
Aspartate aminotransferase (SGOT)	2,410 U/L
Alanine aminotransferase (SGPT)	3,500 U/L

Which of the following pathophysiologic events is most likely occurring in this patient?

- ☐ A. Activation of hepatic stellate cells (5%)
- ☒ B. CD8<sup>+</sup> T-cell response against affected hepatocytes (75%)
- ☐ C. Hepatocyte production of a misfolded protein (1%)
- ☐ D. Neutrophilic infiltration of the liver (15%)
- ☐ E. Plasma cell hepatic migration (1%)

Correct



75%

Answered correctly



47 secs

Time spent



11/15/2020

Last updated

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## Hepatitis A

<b>Clinical presentation</b>	<ul style="list-style-type: none"><li>• Fever, nausea, right upper quadrant pain</li><li>• Jaundice, hepatomegaly</li></ul>
<b>Diagnostic testing</b>	<ul style="list-style-type: none"><li>• Elevated liver transaminases (&gt;1,000 U/L)</li><li>• Anti-hepatitis A serology</li></ul>
<b>Pathology</b>	<ul style="list-style-type: none"><li>• CD8<sup>+</sup> lymphocytes &amp; NK cell response; upregulation of IFN-<math>\gamma</math></li><li>• Microscopic: mononuclear periportal infiltrates, ballooning degeneration of hepatocytes, focal necrosis</li></ul>

IFN- $\gamma$  = interferon-gamma; NK = natural killer.

This patient has **hepatitis A**, a fecal-orally transmitted virus often linked to undercooked shellfish and unsanitary water supplies. Individuals at increased risk include those traveling to endemic areas (eg, South America), homeless shelter residents, and men who have sex with men. Typical manifestations include **fever, jaundice, hepatomegaly**, and leukocytosis. **Liver aminotransferase levels** (eg, alanine aminotransferase [ALT], aspartate aminotransferase [AST]) are dramatically elevated with levels often >1,000 U/L.





>1,000 U/L.

Hepatitis A triggers a robust **CD8<sup>+</sup> lymphocytic** and natural killer cell response to clear infected hepatocytes; the resulting hepatocellular damage is **self-limited**, with complete resolution within 2-3 months. Biopsy is not usually necessary for diagnosis, but typically shows a mononuclear **periportal infiltrate**; ballooning degeneration of hepatocytes and focal necrosis are also sometimes seen in the periportal parenchyma.

**(Choice A)** Chronic hepatic injury due to a variety of causes is associated with stellate cell activation and transformation into collagen-producing myofibroblasts, leading to hepatic fibrosis and cirrhosis. However, although acute hepatic injury in hepatitis A infection may be severe, chronic infection with progression to cirrhosis is rare. Because multiple people have been affected, this patient's infection is likely hepatitis A and not hepatitis B or C, which can progress to chronic liver disease.

**(Choice C)** Alpha-1 antitrypsin (AAT) deficiency causes liver disease characterized by **intracytoplasmic accumulation** of a misfolded and abnormally polymerized AAT protein. However, the onset of symptoms is chronic, fever is not present, and aminotransferase elevations are generally <1,000 U/L. Also, pulmonary symptoms (eg, dyspnea, cough) are common because AAT deficiency also causes early-onset emphysema.





Item 3 of 40

Question Id: 19701



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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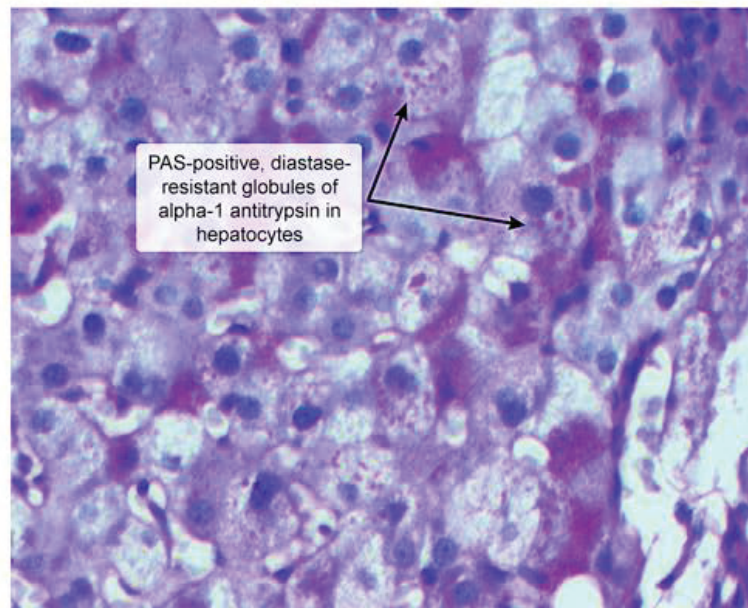
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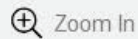
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## Alpha-1 antitrypsin deficiency

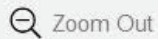


Periodic acid-Schiff (PAS) stain with diastase digestion

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chronic, fever is not present, and aminotransferase elevations are generally  $<1,000$  U/L. Also, pulmonary symptoms (eg, dyspnea, cough) are common because AAT deficiency also causes early-onset emphysema.

**(Choice D)** Histologic findings in alcoholic liver disease include lobular neutrophilic infiltrates, steatosis, ballooning of hepatocytes, and formation of **Mallory-Denk bodies** (eg, cytoplasmic eosinophilic inclusions within hepatocytes). However, aminotransferase elevations are modest and rarely exceed 300 U/L, usually with an AST/ALT ratio  $>2:1$ , which is not present in this patient.

**(Choice E)** **Lymphoplasmacytic infiltration** is characteristic of autoimmune hepatitis. Multiple people would not be affected with similar symptoms if this were the case. Fever is uncommon.

### Educational objective:

Hepatitis A presents with fever, jaundice, hepatomegaly, leukocytosis, and aminotransferase levels  $>1,000$  U/L. It virus triggers a robust CD8<sup>+</sup> lymphocytic response to clear infected hepatocytes. The resulting hepatocellular damage is self-limited, with complete resolution within 2-3 months.

Pathology	Gastrointestinal & Nutrition	Hepatitis a
Subject	System	Topic



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Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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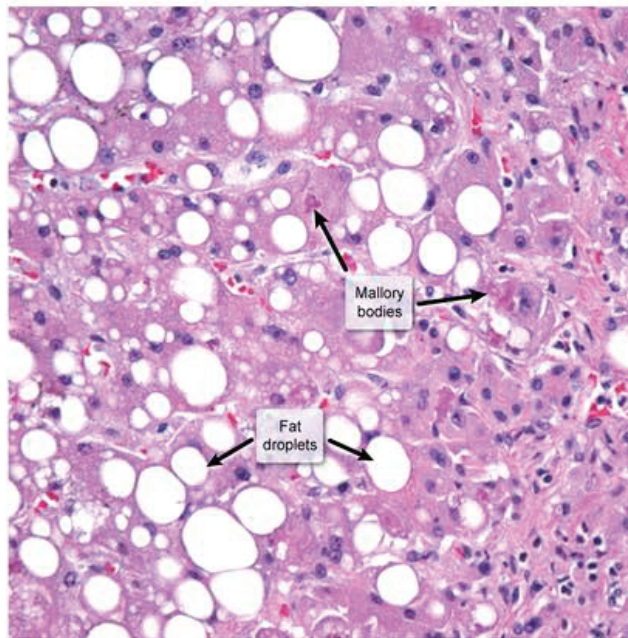
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chronic fever is not present and aminotransferase elevations are generally  $\leq 1,000$  U/L. Also, pulmonary

## Exhibit Display

## Alcoholic liver disease



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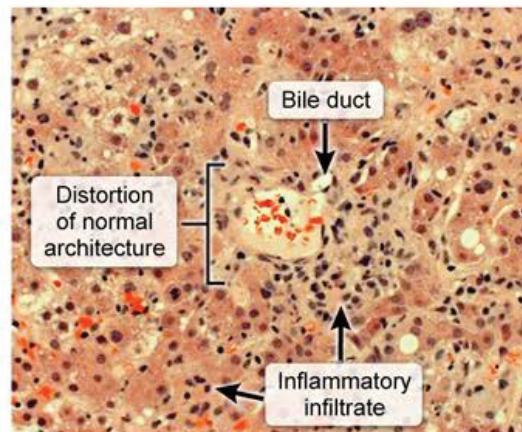
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Normal liver



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Autoimmune hepatitis



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A 54-year-old man comes to the office for evaluation of chronic diarrhea and weight loss. He has had bulky, foul-smelling stools for the past 8 months, which usually occur shortly after eating. There have been no nocturnal bowel movements, and he denies fecal incontinence. The patient also experiences dull, epigastric abdominal pain that is exacerbated by eating and unrelieved by antacids. He drinks 6 or 7 beers a day but denies tobacco or illicit drug use. Vital signs are within normal limits. The abdomen is tender to palpation in the epigastrium without distension, rebound, or guarding. Sudan staining of a fecal specimen is positive, and fecal occult blood testing is negative. Blood testing reveals normal hemoglobin. Which of the following pathophysiologic changes are most likely present in this patient?

- ☐ A. Decreased bile acid synthesis
- ☐ B. Decreased levels of fecal elastase
- ☐ C. Impaired production of intrinsic factor
- ☐ D. Increased pancreatic bicarbonate secretion
- ☐ E. Small bowel villous atrophy





bulky, foul-smelling stools for the past 8 months, which usually occur shortly after eating. There have been no nocturnal bowel movements, and he denies fecal incontinence. The patient also experiences dull, epigastric abdominal pain that is exacerbated by eating and unrelieved by antacids. He drinks 6 or 7 beers a day but denies tobacco or illicit drug use. Vital signs are within normal limits. The abdomen is tender to palpation in the epigastrium without distension, rebound, or guarding. Sudan staining of a fecal specimen is positive, and fecal occult blood testing is negative. Blood testing reveals normal hemoglobin. Which of the following pathophysiologic changes are most likely present in this patient?

- ☐ A. Decreased bile acid synthesis (29%)
- ☒ B. Decreased levels of fecal elastase (40%)
- ☐ C. Impaired production of intrinsic factor (4%)
- ☐ D. Increased pancreatic bicarbonate secretion (7%)
- ☐ E. Small bowel villous atrophy (18%)

Correct



40%

Answered correctly



01 min, 03 secs

Time spent



02/15/2021

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Feedback



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End Block





This patient with a history of alcohol use disorder who has chronic epigastric pain, weight loss, and steatorrhea (ie, bulky, fatty stools) likely has **chronic pancreatitis**, a progressive inflammatory disease that ultimately leads to pancreatic fibrosis. Major risk factors include **alcohol abuse**, recurrent episodes of acute pancreatitis, and smoking.

Patients classically have **epigastric pain** that worsens with meals; pain is initially intermittent but may become constant in advanced disease. Other signs and symptoms of chronic pancreatitis are due to the following pathophysiologic changes:

- **Endocrine insufficiency:** Destruction of islet cells results in insulin-dependent diabetes mellitus.
- **Exocrine insufficiency:** Destruction of acinar cells results in lipase, elastase, amylase, trypsin, and chymotrypsin deficiency. This results in protein and fat malabsorption with **weight loss, steatorrhea**, and fat-soluble vitamin deficiencies.

**Elastase** is derived from a zymogen produced by pancreatic acinar cells and activated by trypsin in the duodenum; levels **correlate with pancreatic exocrine activity**. Therefore, **low fecal elastase** can help diagnose **pancreatic insufficiency** and supports a diagnosis of chronic pancreatitis. Other useful tests include Sudan staining (which identifies fecal fat) and hemoglobin A1c (which diagnoses diabetes mellitus).

(Choice A) Bile acid synthesis, which occurs in the liver, is not affected by chronic pancreatitis. Bile acids



diagnose **pancreatic insufficiency** and supports a diagnosis of chronic pancreatitis. Other useful tests include Sudan staining (which identifies fecal fat) and hemoglobin A1c (which diagnoses diabetes mellitus).

**(Choice A)** Bile acid synthesis, which occurs in the liver, is not affected by chronic pancreatitis. Bile acids are necessary for proper biliary flow; therefore, bile acid synthesis disorders usually present with cholestasis, jaundice, and hepatic failure in neonates.

**(Choice C)** Autoimmune gastritis occurs due to autoantibodies directed at parietal cells and intrinsic factor, resulting in reduced intrinsic factor production. Although patients may have postprandial abdominal pain, they also typically have macrocytic anemia (due to vitamin B<sub>12</sub> deficiency). Steatorrhea (due to fat malabsorption) is unexpected.

**(Choice D)** The pancreas normally produces a bicarbonate-rich fluid that neutralizes stomach acid. Chronic pancreatitis results in progressive pancreatic destruction, leading to decreased pancreatic bicarbonate production.

**(Choice E)** Villous atrophy of the small bowel is characteristic of celiac disease. Although patients can have steatorrhea and abdominal pain, celiac disease also usually causes iron deficiency anemia. In addition, chronic pancreatitis is more likely in this patient with heavy alcohol use.

**Educational objective:**

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### Educational objective:

Chronic pancreatitis is an inflammatory disorder leading to pancreatic fibrosis and atrophy, resulting in endocrine (ie, insulin) and exocrine (eg, lipase, elastase, amylase, trypsin, chymotrypsin) insufficiencies. Patients typically have postprandial steatorrhea (ie, bulky diarrhea that is difficult to flush) and epigastric pain with meals. Low fecal elastase, positive Sudan staining, and elevated hemoglobin A1c support the diagnosis.

### References





A 17-year-old girl is brought to the hospital due to abdominal pain, nausea, and vomiting. She began having periumbilical pain and nausea several hours ago and initially attributed her symptoms to some "bad food" she ate at a potluck lunch earlier in the day. However, her pain progressively worsened and became localized to the right lower quadrant. Temperature is 101 F (38.3 C), blood pressure is 124/78 mm Hg, pulse is 92/min, and respirations are 14/min. On examination, the patient has right lower quadrant tenderness with guarding. Laboratory evaluation shows leukocytosis. Surgical intervention is planned. During surgery, which of the following landmarks is most helpful in identifying the diseased organ?

- ☐ A. Greater omentum
- ☐ B. Haustra of the colon
- ☐ C. Lesser omentum
- ☐ D. Psoas major muscle
- ☐ E. Teniae coli

**Submit**

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- ☐ A. Greater omentum (2%)
- ☐ B. Haustra of the colon (16%)
- ☐ C. Lesser omentum (2%)
- ☐ D. Psoas major muscle (30%)
- ☒ E. Teniae coli (48%)





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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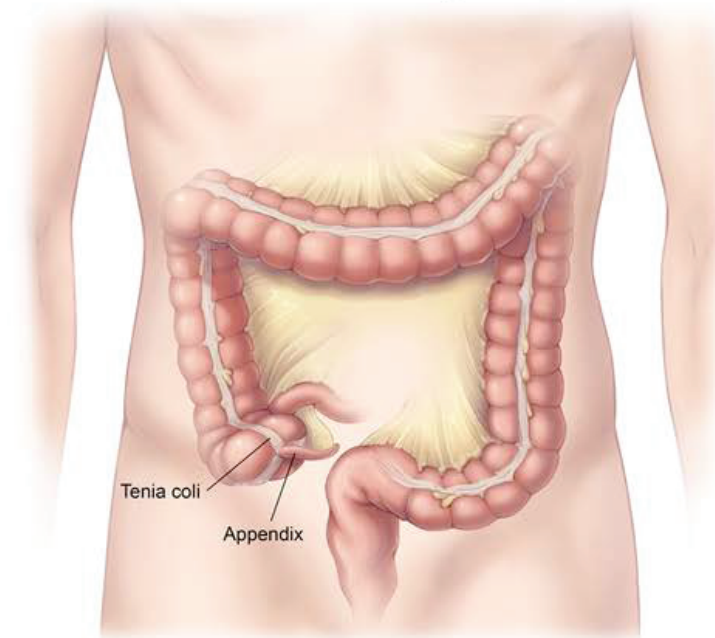
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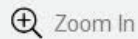
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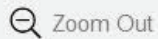
## Colon anatomy



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This patient most likely has **appendicitis**, which is usually treated by removing the appendix. During the procedure, the **teniae coli** can be used as a surgical landmark.

The teniae coli begin as a continuous layer of longitudinal muscle that surrounds the rectum just below the serosa. At the rectosigmoid junction, this layer condenses to form **3 distinct longitudinal bands** that travel on the outside of the entire colon before **converging** at the root of the vermiform **appendix**. The teniae coli have a similar function as the outer layer of the muscularis externa in other portions of the digestive tract. If the appendix cannot be identified by palpation during an appendectomy, it can be located by following the teniae coli to its origin at the cecal base.

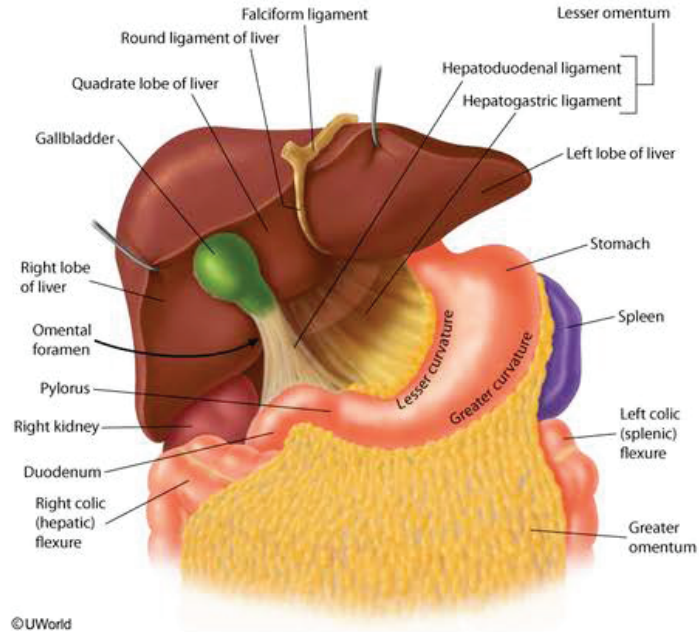
**(Choices A and C)** The greater **omentum** extends from the greater curvature of the stomach in front of the small intestine. It then reflects on itself and ascends to encompass the transverse colon before reaching the posterior abdominal wall. The lesser omentum extends from the fissure of ligamentum venosum and porta hepatis to the lesser curvature of the stomach (hepatogastric ligament) and the start of the duodenum (hepatoduodenal ligament).

**(Choice B)** The teniae coli run the length of the colon and contract lengthwise to form haustra, colonic sacculations causing the colon's segmented appearance. Compared to the circumferential small intestinal





### Exhibit Display

### Greater & lesser omentum




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sacculations causing the colon's segmented appearance. (Compared to the circumferential small intestinal

Block Time Remaining: 00:04:10

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Feedback



Suspend



End Block

(hepatoduodenal ligament).

**(Choice B)** The teniae coli run the length of the colon and contract lengthwise to form haustra, colonic sacculations causing the colon's segmented appearance. Compared to the circumferential small intestinal folds, the distance between haustra is wider and they do not span the entire colonic circumference. These differences help distinguish the colon from the small intestine on abdominal x-ray.

**(Choice D)** Acute appendicitis due to a retrocecal appendix can irritate the iliopsoas group of hip flexors. Psoas sign is abdominal pain elicited by passive thigh extension, which causes friction against nearby inflamed tissues. However, psoas sign can be due to any retroperitoneal irritation and is not specific for appendicitis.

### Educational objective:

The teniae coli are 3 separate smooth muscle ribbons that travel longitudinally on the outside of the colon and converge at the root of the vermiform appendix. If the appendix cannot be identified by palpation during an appendectomy, it can be located by following the teniae coli to their origin at the cecal base.

Anatomy

Gastrointestinal & Nutrition

Appendicitis

Subject

System

Topic

Block Time Remaining: 00:04:10

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A 32-year-old man presents to the emergency department with a one-day history of severe abdominal pain along with nausea and vomiting. His pain is constant and radiates to his back. He admits to “drinking a few beers” with some friends a couple days ago. Laboratory studies reveal significantly elevated amylase and lipase. An abdominal CT shows pancreas divisum, a common congenital anomaly that results from failure of the pancreatic ductal systems of the ventral and dorsal pancreatic primordia to fuse during embryogenesis. Which of the following pancreatic structures is derived from the ventral pancreatic primordium?

- ☐ A. Tail
- ☐ B. Body
- ☐ C. Superior aspect of the head
- ☐ D. Accessory pancreatic duct
- ☐ E. Main pancreatic duct

**Submit**



A 32-year-old man presents to the emergency department with a one-day history of severe abdominal pain along with nausea and vomiting. His pain is constant and radiates to his back. He admits to “drinking a few beers” with some friends a couple days ago. Laboratory studies reveal significantly elevated amylase and lipase. An abdominal CT shows pancreas divisum, a common congenital anomaly that results from failure of the pancreatic ductal systems of the ventral and dorsal pancreatic primordia to fuse during embryogenesis. Which of the following pancreatic structures is derived from the ventral pancreatic primordium?

- ☐ A. Tail (7%)
- ☐ B. Body (5%)
- ☐ C. Superior aspect of the head (22%)
- ☒ D. Accessory pancreatic duct (15%)
- ☒ E. Main pancreatic duct (49%)

Incorrect

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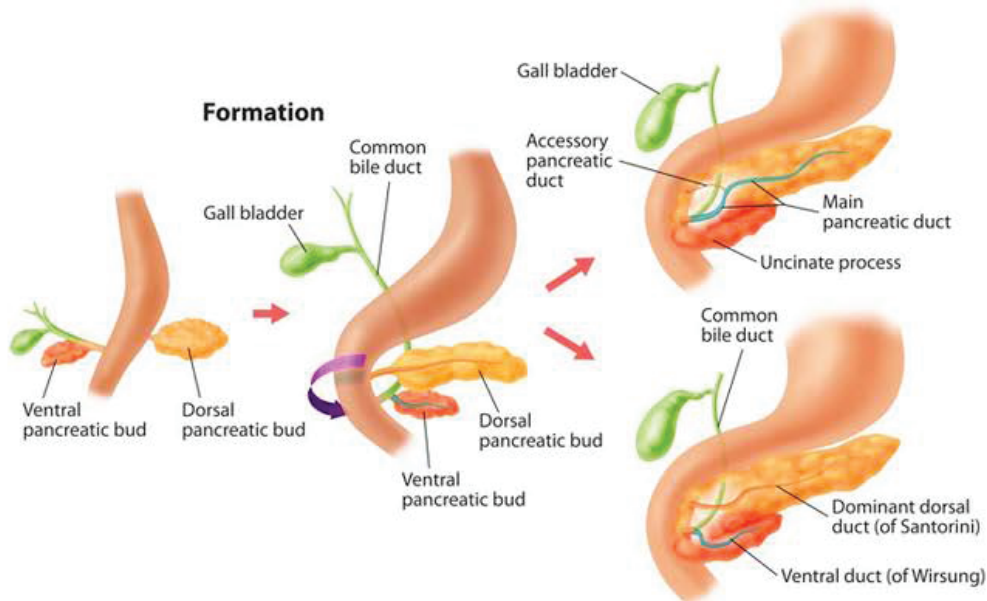


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## Exhibit Display

## Normal Pancreas development



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## Pancreatic divisum



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Early in fetal life, the duodenal portion of the foregut gives rise to the dorsal and ventral pancreatic buds. The dorsal pancreatic bud forms the pancreatic tail, body, most of the head, and the small accessory pancreatic duct. The smaller ventral bud gives rise to the uncinate process, a portion of the pancreatic head, and the proximal portion of the main pancreatic duct. The dorsal and ventral pancreatic buds then fuse during the eighth week of fetal life. The proximal part of the dorsal (accessory) pancreatic duct often degenerates, although it may persist as a functional lesser pancreatic duct. The remainder of the accessory duct fuses with the ventral duct to form the main pancreatic duct (of Wirsung).

***Pancreas divisum*** occurs when the ventral and dorsal pancreatic buds fail to fuse; the pancreatic secretions are instead drained via two separate duct systems. The dominant dorsal duct (of Santorini) opens into the duodenum via the minor papilla, and is responsible for draining the majority of the pancreas. The smaller ventral duct (of Wirsung) opens into the major papilla, and functions to drain the inferior/posterior portion of the head and uncinate process. *Pancreas divisum* is found in 5% of the population and is usually clinically silent. It is commonly detected as an incidental finding on imaging studies or at autopsy. In some, it may predispose to the development of recurrent pancreatitis.

**(Choices A, B, C and D)** The pancreatic tail, body, superior aspect of the head, and accessory pancreatic duct are derivatives of the dorsal pancreatic bud.





opens into the duodenum via the minor papilla, and is responsible for draining the majority of the

pancreas. The smaller ventral duct (of Wirsung) opens into the major papilla, and functions to drain the inferior/posterior portion of the head and uncinuate process. Pancreas divisum is found in 5% of the population and is usually clinically silent. It is commonly detected as an incidental finding on imaging studies or at autopsy. In some, it may predispose to the development of recurrent pancreatitis.

**(Choices A, B, C and D)** The pancreatic tail, body, superior aspect of the head, and accessory pancreatic duct are derivatives of the dorsal pancreatic bud.

### Educational objective:

The dorsal pancreatic bud forms the majority of pancreatic tissue (body, tail, and most of the head). The ventral pancreatic bud is a precursor of the uncinuate process, inferior/posterior portion of the head, and major pancreatic duct (of Wirsung). Failure of the dorsal and ventral pancreatic buds to fuse leads to pancreas divisum. In this condition, the pancreatic ductal systems remain separate, with the accessory duct draining the majority of the pancreas.

### References

- [Clinical significance of the accessory pancreatic duct.](#)

Embryology

Gastrointestinal & Nutrition

Acute pancreatitis

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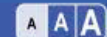
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A term newborn boy is evaluated in the neonatal intensive care unit for respiratory distress. Apgar scores are 2 and 5 at 1 and 5 minutes, respectively. Respirations are 84/min. On examination, the patient has a barrel chest with a scaphoid abdomen and mild cyanosis of his extremities. Auscultation shows absent breath sounds on the left; right lung aeration is normal. Chest x-ray reveals multiple fluid-containing cystic areas on the left and a mediastinal shift to the right. Which of the following embryologic events most likely failed to occur in this patient?

- ☐ A. Closure of the pleuroperitoneal fold
- ☐ B. Closure of the ventral body wall
- ☐ C. Formation of the pleuropericardial membrane
- ☐ D. Rotation of the midgut
- ☐ E. Separation of the dorsal and ventral foregut

**Submit**





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- ✓ ☒ A. Closure of the pleuroperitoneal fold (73%)
- ☐ B. Closure of the ventral body wall (3%)
- ☐ C. Formation of the pleuropericardial membrane (15%)
- ☐ D. Rotation of the midgut (4%)
- ☐ E. Separation of the dorsal and ventral foregut (4%)

Correct



73%

Answered correctly



39 secs

Time Spent



11/08/2020

Last Updated

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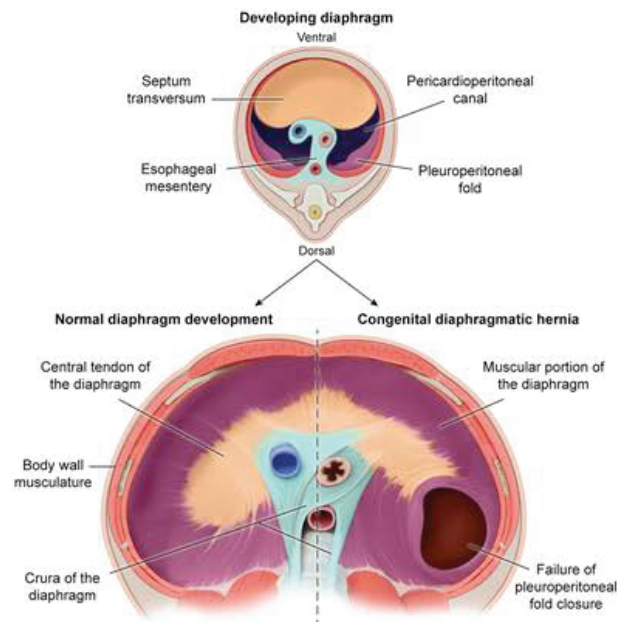


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## Exhibit Display

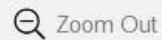
## Congenital diaphragmatic hernia



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This **newborn** with **respiratory distress** and **unilateral decreased breath sounds** has a **scaphoid abdomen** and **chest x-ray** revealing cystic structures. These findings are consistent with a **congenital diaphragmatic hernia** (CDH), a congenital malformation caused by failure of the pleuroperitoneal folds to close.

In general, the diaphragm forms from 4 distinct tissues: the septum transversum, esophageal mesentery, musculature from the body wall, and pleuroperitoneal folds. Extension of the **pleuroperitoneal folds** to these other structures ultimately leads to division of the pericardioperitoneal canal into the peritoneal cavity and thoracic cavity. **Failure of closure** results in an abnormal communication between the thorax and abdomen. This defect is usually located on the **left posterolateral side**, allowing bowel, stomach, spleen, and/or liver to herniate into the thorax. Because this malformation occurs during organogenesis in the first trimester, compression of the developing lung leads to **pulmonary hypoplasia**.

Affected newborns have respiratory distress at birth. Displacement of abdominal organs into the thorax causes the abdomen to appear scaphoid and the chest barrel shaped. Ipsilateral breath sounds are decreased or absent. Chest x-ray findings supportive of CDH include **mediastinal shift** and **thoracic**

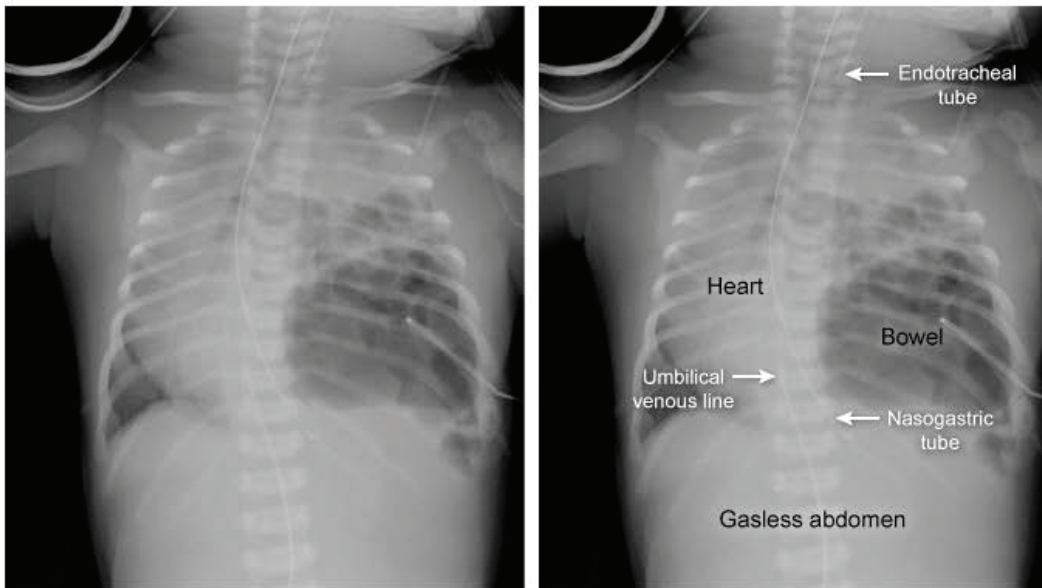




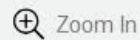
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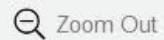
## Congenital diaphragmatic hernia



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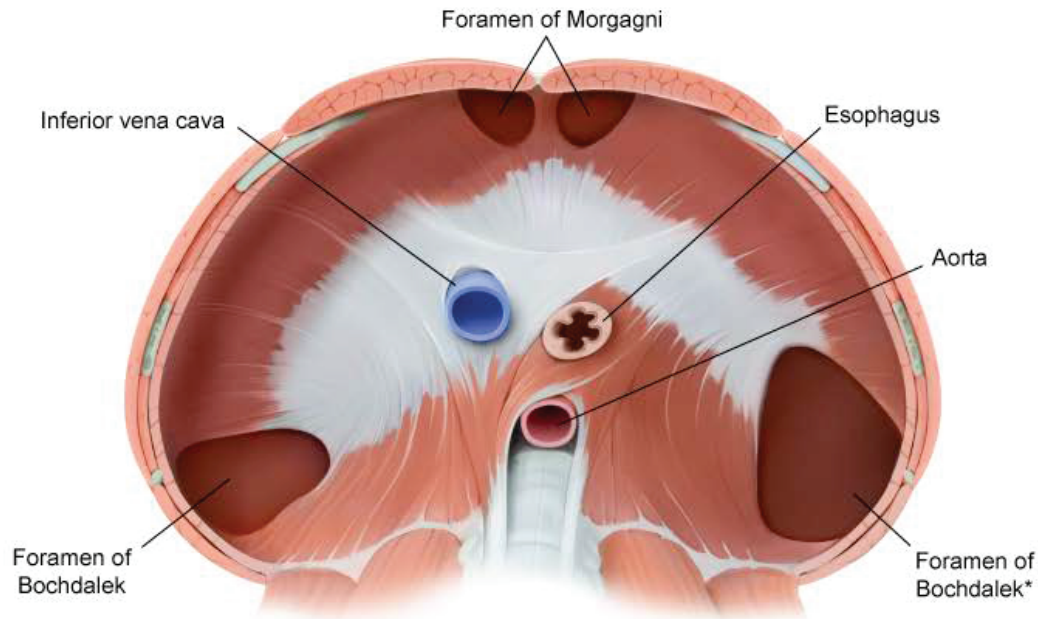
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decreased or absent. Chest x-ray findings supportive of CDH include mediastinal shift and thoracic

## Exhibit Display

## Sites of congenital diaphragmatic herniation



\*Left sided posterolateral herniation is most common

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decreased or absent. Chest x-ray findings supportive of CDH include mediastinal shift and thoracic

**bowel loops**, which may appear as cystic, fluid-filled structures.

**(Choice B)** Failure of ventral body wall closure results in **gastroschisis**, which is characterized by bowel evisceration without a protective membrane. A full-thickness abdominal wall defect is apparent on examination.

**(Choice C)** The pleuropericardial membranes, which become the fibrous pericardium, fuse to separate the pericardial and pleural cavities. Fusion defects are rare, often asymptomatic, and result in communication between these two thoracic cavities, not between the thorax and abdomen.

**(Choice D)** **Malrotation**, characterized by incomplete physiologic rotation of the bowel in utero, usually presents with bilious emesis in infancy due to duodenal obstruction from abnormally positioned peritoneal bands. Respiratory distress and thoracic bowel loops would not be seen.

**(Choice E)** Abnormal separation of the dorsal (gastrointestinal tract) and ventral (respiratory tract) foregut results in **esophageal atresia** with or without a tracheoesophageal fistula. Symptoms include respiratory distress and choking with feeds; chest x-ray would not show cystic thoracic structures.

### Educational objective:

Congenital diaphragmatic hernia is caused by failure of the pleuroperitoneal folds to close. Immediately





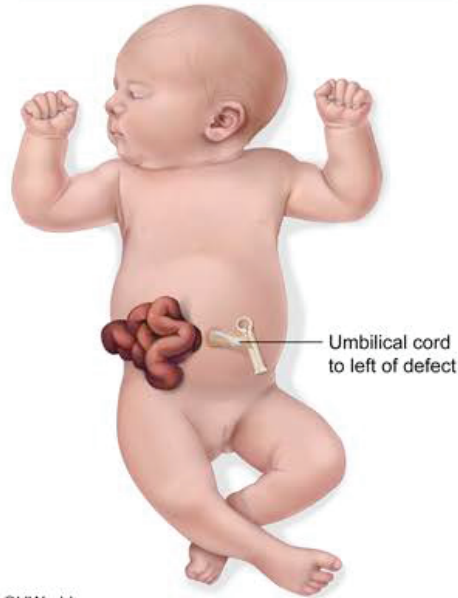


decreased or absent. Chest x-ray findings supportive of CDH include mediastinal shift and thoracic

### Exhibit Display

#### Gastroschisis

Eviscerated bowel with no covering membrane



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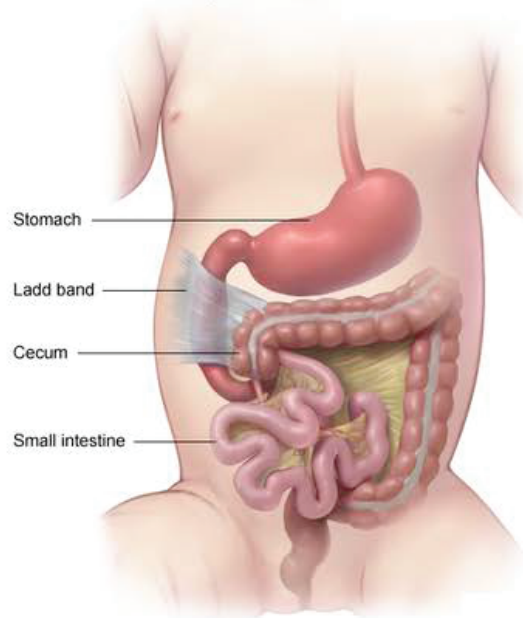




decreased or absent. Chest x-ray findings supportive of CDH include mediastinal shift and thoracic

### Exhibit Display

#### Midgut malrotation



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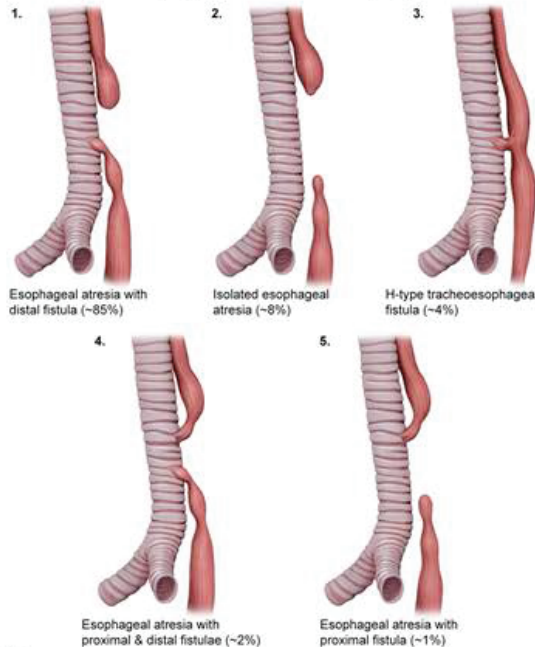
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decreased or absent. Chest x-ray findings supportive of CF include mediastinal shift and thoracic

## Exhibit Display

## Types of esophageal atresia &amp; tracheoesophageal fistula



Zoom In

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pericardial and pleural cavities. Fusion defects are rare, often asymptomatic, and result in communication between these two thoracic cavities, not between the thorax and abdomen.

**(Choice D)** [Malrotation](#), characterized by incomplete physiologic rotation of the bowel in utero, usually presents with bilious emesis in infancy due to duodenal obstruction from abnormally positioned peritoneal bands. Respiratory distress and thoracic bowel loops would not be seen.

**(Choice E)** Abnormal separation of the dorsal (gastrointestinal tract) and ventral (respiratory tract) foregut results in [esophageal atresia](#) with or without a tracheoesophageal fistula. Symptoms include respiratory distress and choking with feeds; chest x-ray would not show cystic thoracic structures.

### Educational objective:

Congenital diaphragmatic hernia is caused by failure of the pleuroperitoneal folds to close. Immediately after birth, newborns have respiratory distress, unilateral decreased breath sounds, and a scaphoid abdomen, with imaging revealing thoracic bowel loops and mediastinal shift.

### References

- [Congenital diaphragmatic hernia.](#)
- [Congenital diaphragmatic hernia—a review.](#)





A 22-year-old male presents to the emergency department complaining of fever, abdominal pain, and vomiting. He has had these symptoms for the past four days, but has not sought medical attention because of concerns over the cost of treatment. On examination, the patient appears acutely ill. There is right lower quadrant tenderness with rebound as well as a palpable mass. CT scan of the abdomen and pelvis demonstrates a periappendiceal fluid collection. Culture of this fluid would most likely isolate which of the following organisms?

- ☐ A. *Staphylococcus aureus*
- ☐ B. *Actinomyces*
- ☐ C. *Candida albicans*
- ☐ D. *Bacteroides fragilis*
- ☐ E. *Entamoeba histolytica*

Submit





A 22-year-old male presents to the emergency department complaining of fever, abdominal pain, and vomiting. He has had these symptoms for the past four days, but has not sought medical attention because of concerns over the cost of treatment. On examination, the patient appears acutely ill. There is right lower quadrant tenderness with rebound as well as a palpable mass. CT scan of the abdomen and pelvis demonstrates a periappendiceal fluid collection. Culture of this fluid would most likely isolate which of the following organisms?

- ☐ A. *Staphylococcus aureus* (13%)
- ☐ B. *Actinomyces* (3%)
- ☐ C. *Candida albicans* (0%)
- ☒ D. *Bacteroides fragilis* (73%)
- ☐ E. *Entamoeba histolytica* (9%)

Correct



73%

Answered correctly



46 secs

Time Spent



11/15/2020

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Feedback



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End Block





This patient is suffering from perforated appendicitis that has evolved into an intraabdominal abscess.

Although most infections within the abdominal cavity are polymicrobial, *B. fragilis* is a common anaerobic gram-negative bacillus that is frequently isolated, and of the choices given, it is the most likely organism to be identified in the culture of this patient's abscess. This organism expresses unique surface polysaccharides that have been shown to favor abscess formation. In addition to *B. fragilis*, common bacterial isolates from intraabdominal infections include other members of the normal colonic flora such as *Escherichia coli*, enterococci, and streptococci.

**(Choice A)** *S. aureus* is a gram-positive organism that can cause abscess formation on the skin, but is not typically isolated from an intraabdominal abscess.

**(Choice B)** *Actinomyces* species are anaerobic bacteria that can form abscesses in the cervicofacial region or abdominal cavity. However, they are much less common than *B. fragilis* and typically do not form abscesses this quickly.

**(Choice C)** *Candida albicans* can be isolated from an infection resulting from perforation of the proximal bowel such as a perforated peptic ulcer.

**(Choice E)** Infection with *E. histolytica* can result in the formation of an amebic liver abscess. This patient, however, has perforated appendicitis, which is not related to infection with *E. histolytica*.





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Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

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(Choice A) *C. aureus* is a gram-positive organism that can cause abscess formation on the skin, but is not typically isolated from an intraabdominal abscess.

(Choice B) *Actinomyces* species are anaerobic bacteria that can form abscesses in the cervicofacial region or abdominal cavity. However, they are much less common than *B. fragilis* and typically do not form abscesses this quickly.

(Choice C) *Candida albicans* can be isolated from an infection resulting from perforation of the proximal bowel such as a perforated peptic ulcer.

(Choice E) Infection with *E. histolytica* can result in the formation of an amebic liver abscess. This patient, however, has perforated appendicitis, which is not related to infection with *E. histolytica*.

### Educational objective:

Intraabdominal infections are polymicrobial, with *B. fragilis* and *E. coli* being the most prominent organisms isolated.

Microbiology

Subject

Gastrointestinal &amp; Nutrition

System

Appendicitis

Topic

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A 34-year-old woman comes to the office with recent onset of malaise. The patient reports feeling "run down and under the weather" but otherwise has no symptoms. She is an avid cyclist and is concerned about her ability to participate in a charity race in 3 days. The patient works as a nurse at a local hospital and lives at home with her husband and 2-year-old son. She occasionally smokes when she goes out, but since she began feeling ill, she no longer has the desire to smoke. Physical examination is notable for hepatomegaly. Laboratory results are as follows:

Anti-HAV IgM	positive
Anti-HAV IgG	negative
HBsAg	negative
HBeAg	negative
Anti-HBs	positive
Anti-HBc	negative
Anti-HBe	negative
Anti-HCV	negative







Anti-HBs	positive
Anti-HBc	negative
Anti-HBe	negative
Anti-HCV	negative

Which of the following is most likely to be elicited on further history taking?

- ☐ A. Had a tattoo recently at a local tattoo parlor
- ☐ B. Had an accidental needlestick exposure at work
- ☐ C. Had boiled eggs from the hospital cafeteria
- ☐ D. Had steamed oysters at a neighborhood restaurant
- ☐ E. Had unprotected sexual intercourse with a new partner

Submit





Anti-HBs	positive
Anti-HBc	negative
Anti-HBe	negative
Anti-HCV	negative

Which of the following is most likely to be elicited on further history taking?

- ☐ A. Had a tattoo recently at a local tattoo parlor (1%)
- ☐ B. Had an accidental needlestick exposure at work (10%)
- ☐ C. Had boiled eggs from the hospital cafeteria (8%)
- ☒ D. Had steamed oysters at a neighborhood restaurant (75%)
- ☐ E. Had unprotected sexual intercourse with a new partner (3%)

Correct

75%



25 secs



01/15/2021

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**Hepatitis A** infection is caused by an RNA picornavirus with an average incubation period of 30 days. Transmission occurs through the **fecal-oral** route and is common in areas with overcrowding and poor sanitation. Outbreaks frequently result from **contaminated water or food**, with raw or steamed **shellfish** being the typical (and classically tested) culprit in the United States. Onset is acute, and symptoms can include malaise, fatigue, anorexia, nausea, vomiting, mild abdominal pain, and an aversion to smoking (for unclear reasons). Hepatomegaly is commonly seen. Serum aminotransferases spike early in the illness, followed by increases in bilirubin and alkaline phosphatase. Anti-HAV IgM is positive and is a marker of active disease. Hepatitis A infection is a self-limiting disease and does not progress to chronic hepatitis, cirrhosis, or hepatocellular carcinoma.

Treatment is largely supportive, with complete recovery expected in 3-6 weeks. People considered at high risk (eg, those living in or traveling to endemic areas, those with chronic liver disease or clotting factor disorders, men who have sex with men) should be given the hepatitis A vaccine as prophylaxis.

Unvaccinated close contacts of individuals with hepatitis A should receive the vaccine or immune globulin.

**(Choices A, B, and E)** Unsanitary tattooing (eg, with contaminated needles), accidental needlesticks, and unprotected sexual intercourse are important risk factors for hepatitis B and C. This patient is positive for HBsAb, which confirms that she has antibodies to hepatitis B surface antigen and, given the negative anti-







Unvaccinated close contacts of individuals with hepatitis A should receive the vaccine or immune globulin.

**(Choices A, B, and E)** Unsanitary tattooing (eg, with contaminated needles), accidental needlesticks, and unprotected sexual intercourse are important risk factors for hepatitis B and C. This patient is positive for HBsAb, which confirms that she has antibodies to hepatitis B surface antigen and, given the negative anti-HBc, suggests that she has been vaccinated and is now immune.

**(Choice C)** The consumption of boiled eggs is not commonly associated with hepatitis A infection. If the boiled eggs were insufficiently cooked, *Salmonella* infection would be a risk.

### Educational objective:

Transmission of the hepatitis A virus occurs through the fecal-oral route and is common in areas with overcrowding and poor sanitation. Outbreaks frequently result from contaminated water or food, and raw or steamed shellfish is a common culprit in the United States.

### References

- [Risk assessment in shellfish-borne outbreaks of hepatitis A.](#)

Microbiology

Gastrointestinal &amp; Nutrition

Hepatitis a

Subject

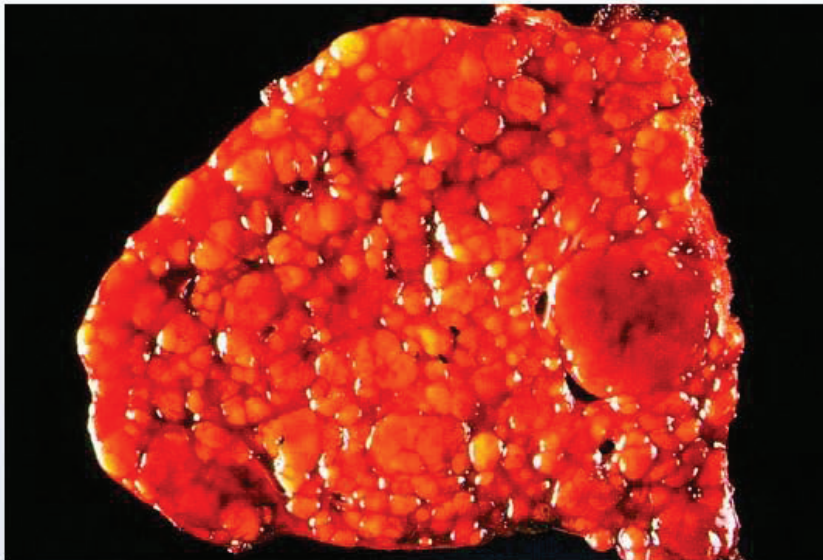
System

Topic



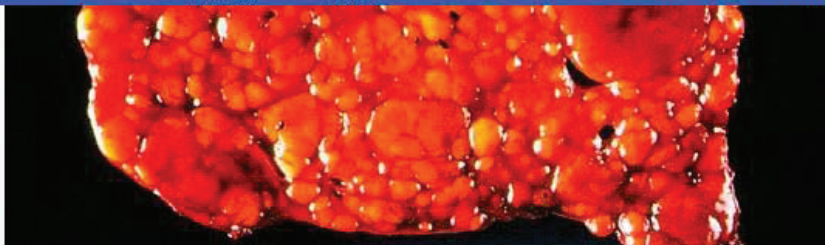


A 54-year-old man dies from profuse upper gastrointestinal hemorrhage. An autopsy is performed; gross examination of his liver is shown in the image below.



This patient's condition most likely resulted from which of the following processes?





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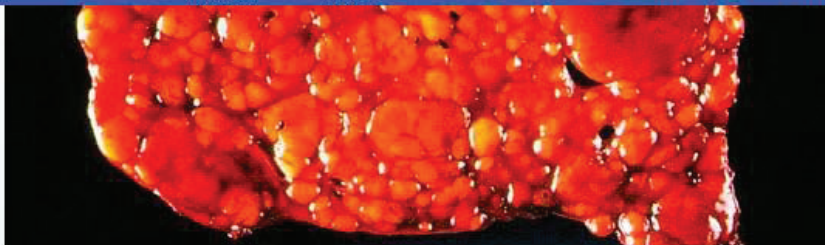
This patient's condition most likely resulted from which of the following processes?

- ☐ A. Dilation of sinusoids and perivenular hemorrhages
- ☐ B. Fibrosis and nodular parenchymal regeneration
- ☐ C. Granulomatous destruction of bile ducts
- ☐ D. Intrahepatic hydatid cysts with surrounding fibrous reaction
- ☐ E. Pigment accumulation within hepatocytes

Submit







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This patient's condition most likely resulted from which of the following processes?

- ☐ A. Dilation of sinusoids and perivenular hemorrhages (17%)
- ☒ B. Fibrosis and nodular parenchymal regeneration (71%)
- ☐ C. Granulomatous destruction of bile ducts (2%)
- ☐ D. Intrahepatic hydatid cysts with surrounding fibrous reaction (7%)
- ☐ E. Pigment accumulation within hepatocytes (1%)

Correct

71%  
Answered correctly

56 secs  
Time spent

12/11/2020  
Last updated

Block Time Remaining: 00:07:11

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End Block



**Cirrhosis**, the end stage of many chronic liver diseases, is characterized by **diffuse hepatic fibrosis** with replacement of the normal lobular architecture by fibrous-lined **regenerative parenchymal nodules**. The most common causes include **chronic viral hepatitis** (eg, hepatitis B and C), **alcohol**, hemochromatosis, and nonalcoholic fatty liver disease. **Portal hypertension**, from increased resistance to hepatic blood flow, typically develops in advanced cirrhosis and can lead to development of **gastroesophageal varices**. Untreated, these varices are prone to rupture and can result in a massive gastrointestinal hemorrhage and possibly death.

**(Choice A)** Dilation of sinusoids and perivenular hemorrhage are associated with acute venous outflow obstruction within the liver (eg, Budd-Chiari syndrome). Chronic hepatic vein obstruction is a rare cause of cirrhosis and portal hypertension.

**(Choice C)** Granulomatous destruction of bile ducts is seen in patients with primary biliary cirrhosis (PBC). Although PBC can cause cirrhosis, it is a far less common cause than alcohol or chronic hepatitis. Moreover, PBC occurs almost exclusively in women.

**(Choice D)** Intrahepatic hydatid cysts with surrounding fibrous reaction can be seen in patients with an *Echinococcus* infection, but it is a very rare disease in the United States.

**(Choice E)** Pigment accumulation within hepatocytes occurs in conditions such as Dubin-Johnson







Item 10 of 40

Question Id: 368



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

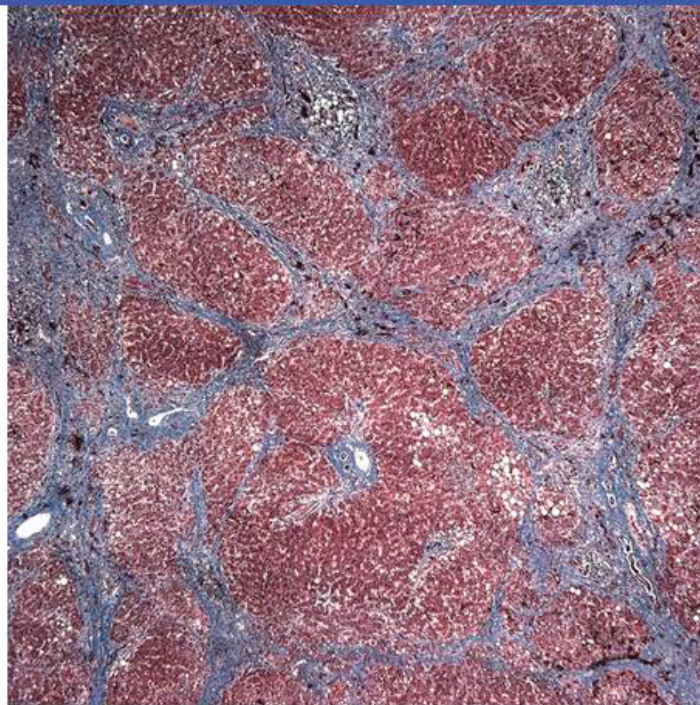


Text Zoom



Settings

### Exhibit Display



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(Choice 5) Pigment accumulation within hepatocytes occurs in conditions such as Dubin-Johnson

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Feedback

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(PBC). Although PBC can cause cirrhosis, it is a far less common cause than alcohol or chronic hepatitis.

Moreover, PBC occurs almost exclusively in women.

**(Choice D)** Intrahepatic hydatid cysts with surrounding fibrous reaction can be seen in patients with an *Echinococcus* infection, but it is a very rare disease in the United States.

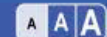
**(Choice E)** Pigment accumulation within hepatocytes occurs in conditions such as Dubin-Johnson syndrome, an autosomal recessive disorder causing conjugated hyperbilirubinemia. In this condition, hepatocellular accumulation of coarse pigmented granules causes the liver to appear grossly black.

### Educational objective:

Cirrhosis is characterized by diffuse hepatic fibrosis with replacement of the normal lobular architecture by fibrous-lined parenchymal nodules. Chronic viral hepatitis (eg, hepatitis B and C), alcohol, hemochromatosis, and nonalcoholic fatty liver disease are the most common causes of cirrhosis in the United States.

Pathology	Gastrointestinal & Nutrition	Cirrhosis
Subject	System	Topic

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A 42-year-old woman comes to the office with persistent hyperlipidemia despite 6 months of maintaining a healthy diet and exercising regularly. Although her past medical history is significant for biliary colic secondary to gallstones, the patient has refused elective cholecystectomy. Her father died of a myocardial infarction at age 54, and her mother has diabetes mellitus. The patient's temperature is 36.1 C (97 F), blood pressure is 122/79 mm Hg, pulse is 78/min, and respirations are 14/min. Examination shows no abnormalities. Laboratory studies obtained 1 week ago show elevated serum triglycerides and LDL cholesterol levels. Drug therapy is discussed with the patient. Given this patient's preexisting gallbladder disease, which of the following drugs should be avoided?

- ☐ A. Atorvastatin
- ☐ B. Ezetimibe
- ☐ C. Fish oil
- ☐ D. Gemfibrozil
- ☐ E. Niacin





healthy diet and exercising regularly. Although her past medical history is significant for **biliary colic** secondary to gallstones, the patient has refused elective cholecystectomy. Her father died of a myocardial infarction at age 54, and her mother has diabetes mellitus. The patient's temperature is 36.1 C (97 F), blood pressure is 122/79 mm Hg, pulse is 78/min, and respirations are 14/min. Examination shows no abnormalities. Laboratory studies obtained 1 week ago show elevated serum triglycerides and LDL cholesterol levels. Drug therapy is discussed with the patient. Given this patient's preexisting gallbladder disease, which of the following drugs should be avoided?

- ☐ A. Atorvastatin (7%)
- ☐ B. Ezetimibe (18%)
- ☐ C. Fish oil (4%)
- ☒ D. Gemfibrozil (64%)
- ☐ E. Niacin (6%)

Correct

64%



57 secs



01/11/2021

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Feedback



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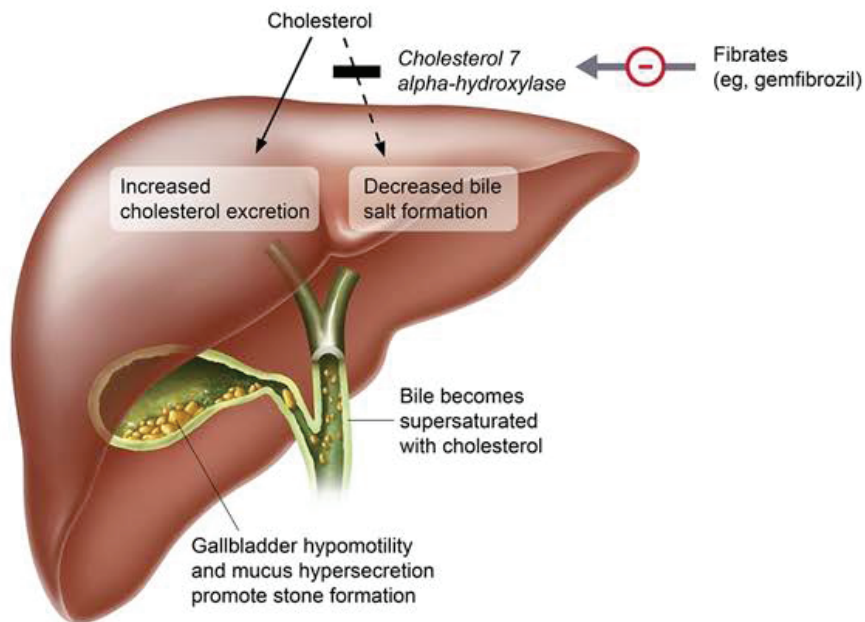
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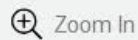


## Exhibit Display

## Formation of cholesterol gallstones



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In patients with significant **hypertriglyceridemia**, fibrates are particularly effective due to their ability to upregulate lipoprotein lipase resulting in increased oxidation of fatty acids (liver, muscles). Gemfibrozil and other **fibrates** inhibit the rate-limiting enzyme in bile acid synthesis, cholesterol 7-alpha-hydroxylase. The reduced bile acid production results in **decreased cholesterol solubility** and increased microcrystal precipitation, thereby **promoting gallstone formation**. As a result, fibrates should be used with caution in patients with preexisting gallbladder disease. Patients on fibrate therapy should also be monitored for myopathy, a risk significantly increased when fibrates are used concurrently with statins.

**(Choice A)** Long-term use of statins (eg, atorvastatin) is associated with decreased risk of gallstone disease as inhibition of HMG-CoA reductase reduces cholesterol biosynthesis and bile supersaturation. Side effects of statin therapy include hepatic dysfunction (elevated aminotransferases) and myopathy.

**(Choice B)** Ezetimibe blocks intestinal cholesterol absorption, decreasing liver cholesterol stores and reducing biliary cholesterol content. Adverse effects associated with ezetimibe include elevated transaminases (increased with concurrent use of statins) and diarrhea.

**(Choice C)** Fish oil supplements containing high concentrations of omega-3 fatty acids increase bile acid synthesis, decrease cholesterol saturation in bile, and increase gallbladder motility. The net effect is a decreased risk of gallstone formation.



reducing biliary cholesterol content. Adverse effects associated with ezetimibe include elevated transaminases (increased with concurrent use of statins) and diarrhea.

**(Choice C)** Fish oil supplements containing high concentrations of omega-3 fatty acids increase bile acid synthesis, decrease cholesterol saturation in bile, and increase gallbladder motility. The net effect is a decreased risk of gallstone formation.

**(Choice E)** Niacin increases HDL (via reduced catabolism) and lowers triglyceride levels (through inhibition of VLDL secretion). It is associated with lower rates of gallstone disease. Niacin commonly promotes flushing, a temporary prostaglandin-mediated effect often blunted by use of nonsteroidal anti-inflammatory drugs.

### Educational objective:

Gemfibrozil (and other fibrates) can reduce cholesterol solubility and promote gallstone formation by reducing bile acid synthesis. Caution should be used when prescribing fibrate therapy to patients with underlying gallbladder disease.

### References

- [Triglycerides and gallstone formation.](#)





A 50-year-old woman comes to the physician due to periodic reddening of her skin that is starting to become bothersome. The redness involves mainly her face and neck and is accompanied by mild warmth. The episodes initially lasted only a few minutes, but now they sometimes exceed 20 minutes. The patient has also had persistent watery diarrhea and associated abdominal cramping for the last several months. Physical examination shows several, purple vascular lesions surrounding her nose. Urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) over 24 hours is increased. Abdominal imaging shows a tumor in the small intestine. Which of the following is most likely responsible for this patient's condition?

- ☐ A. Localized adenocarcinoma
- ☐ B. Localized carcinoid
- ☐ C. Metastatic carcinoid
- ☐ D. Metastatic lymphoma
- ☐ E. Secretory leiomyoma

**Submit**

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Feedback



Suspend



End Block



A 50-year-old woman comes to the physician due to periodic reddening of her skin that is starting to become bothersome. The redness involves mainly her face and neck and is accompanied by mild warmth. The episodes initially lasted only a few minutes, but now they sometimes exceed 20 minutes. The patient has also had persistent watery diarrhea and associated abdominal cramping for the last several months. Physical examination shows several, purple vascular lesions surrounding her nose. Urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) over 24 hours is increased. Abdominal imaging shows a tumor in the small intestine. Which of the following is most likely responsible for this patient's condition?

- ☐ A. Localized adenocarcinoma (2%)
- ☐ B. Localized carcinoid (21%)
- ☒ C. Metastatic carcinoid (72%)
- ☐ D. Metastatic lymphoma (2%)
- ☐ E. Secretory leiomyoma (1%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Features of carcinoid syndrome

<b>Clinical manifestations</b>	<ul style="list-style-type: none"><li>• Skin: <b>Flushing</b>, telangiectasias, cyanosis</li><li>• Gastrointestinal: <b>Watery diarrhea</b>, cramping</li><li>• Pulmonary: <b>Bronchospasm</b>, dyspnea, wheezing</li><li>• Cardiac: Valvular fibrous plaques (right &gt; left)</li></ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"><li>• Elevated 24-hour urinary excretion of <b>5-HIAA</b></li><li>• CT/MRI of abdomen &amp; pelvis to localize tumor</li></ul>
<b>Treatment</b>	<ul style="list-style-type: none"><li>• Octreotide for symptomatic patients</li><li>• Surgery for liver metastases</li></ul>

5-HIAA = 5-hydroxyindoleacetic acid.

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**Carcinoid tumors** most frequently arise from the enterochromaffin (endocrine) cells of the intestinal mucosa. These cells produce a number of vasoactive substances, such as serotonin (5-HT), bradykinin, and prostaglandins. When the tumor is confined to the intestine, these secretory products are metabolized by the liver and patients do not develop carcinoid syndrome. In contrast, if intestinal carcinoid **metastasizes to the liver**, these vasoactive substances bypass the liver and enter the systemic



1



Feedback



Suspend



End Block





**Carcinoid tumors** most frequently arise from the enterochromaffin (endocrine) cells of the intestinal mucosa. These cells produce a number of vasoactive substances, such as serotonin (5-HT), bradykinin, and prostaglandins. When the tumor is confined to the intestine, these secretory products are metabolized by the liver and patients do not develop carcinoid syndrome. In contrast, if intestinal carcinoid **metastasizes to the liver**, these vasoactive substances bypass the liver and enter the systemic circulation, resulting in **carcinoid syndrome**. Extraintestinal carcinoid tumors (eg, bronchial carcinoid) can cause carcinoid syndrome without metastasizing as the vasoactive substances are secreted directly into systemic circulation (again bypassing hepatic metabolism).

Increased level of the serotonin metabolite **5-hydroxyindoleacetic acid (5-HIAA)** in a 24-hour urine sample is the most useful initial test for confirming carcinoid syndrome.

**(Choices A, D, and E)** Adenocarcinoma, lymphoma, and secretory leiomyoma would not result in carcinoid syndrome or elevated urinary 5-HIAA levels.

**(Choice B)** The vasoactive substances secreted by a localized intestinal carcinoid tumor are metabolized by the liver via first-pass metabolism, preventing the development of carcinoid syndrome. Extraintestinal metastasis of intestinal carcinoid tumors is required to produce carcinoid symptoms.

**Educational objective:**





cause carcinoid syndrome without metastasizing as the vasoactive substances are secreted directly into systemic circulation (again bypassing hepatic metabolism).

Increased level of the serotonin metabolite **5-hydroxyindoleacetic acid (5-HIAA)** in a 24-hour urine sample is the most useful initial test for confirming carcinoid syndrome.

**(Choices A, D, and E)** Adenocarcinoma, lymphoma, and secretory leiomyoma would not result in carcinoid syndrome or elevated urinary 5-HIAA levels.

**(Choice B)** The vasoactive substances secreted by a localized intestinal carcinoid tumor are metabolized by the liver via first-pass metabolism, preventing the development of carcinoid syndrome. Extraintestinal metastasis of intestinal carcinoid tumors is required to produce carcinoid symptoms.

### Educational objective:

Carcinoid tumors confined to the intestine do not cause carcinoid syndrome as their secretory products are metabolized by the liver before entering the systemic circulation. In contrast, intestinal carcinoids that metastasize to the liver and extraintestinal (eg, bronchial) carcinoids release vasoactive substances that avoid first-pass metabolism, resulting in carcinoid syndrome (eg, flushing, diarrhea, bronchospasm).

Pathophysiology

Gastrointestinal & Nutrition

Carcinoid tumors





A 54-year-old woman is evaluated in the clinic for exertional dyspnea and easy fatigability. The patient has no chest pain, cough, or wheezing. She does not use tobacco, alcohol, or illicit drugs. On physical examination, her gait is unstable when her eyes are closed and there is impaired vibratory sensation in the lower extremities. Marked pallor of the conjunctivae, nail beds, and palms is present. Which of the following laboratory tests would help confirm the most likely diagnosis in this patient?

- ☐ A. Erythrocyte glucose-6-phosphate dehydrogenase activity
- ☐ B. Erythrocyte glutathione reductase activity
- ☐ C. Erythrocytic pyruvate kinase activity
- ☐ D. Erythrocyte transketolase activity
- ☐ E. Serum methylmalonic acid level
- ☐ F. Serum protoporphyrin level

**Submit**





A 54-year-old woman is evaluated in the clinic for exertional dyspnea and easy fatigability. The patient has no chest pain, cough, or wheezing. She does not use tobacco, alcohol, or illicit drugs. On physical examination, her gait is unstable when her eyes are closed and there is impaired vibratory sensation in the lower extremities. Marked pallor of the conjunctivae, nail beds, and palms is present. Which of the following laboratory tests would help confirm the most likely diagnosis in this patient?

- ☐ A. Erythrocyte glucose-6-phosphate dehydrogenase activity (5%)
- ☐ B. Erythrocyte glutathione reductase activity (4%)
- ☐ C. Erythrocytic pyruvate kinase activity (3%)
- ☐ D. Erythrocyte transketolase activity (6%)
- ☒ E. Serum methylmalonic acid level (72%)
- ☐ F. Serum protoporphyrin level (7%)

Correct



72%

Answered correctly



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01/24/2021

Last Updated

Block Time Remaining: 00:08:51

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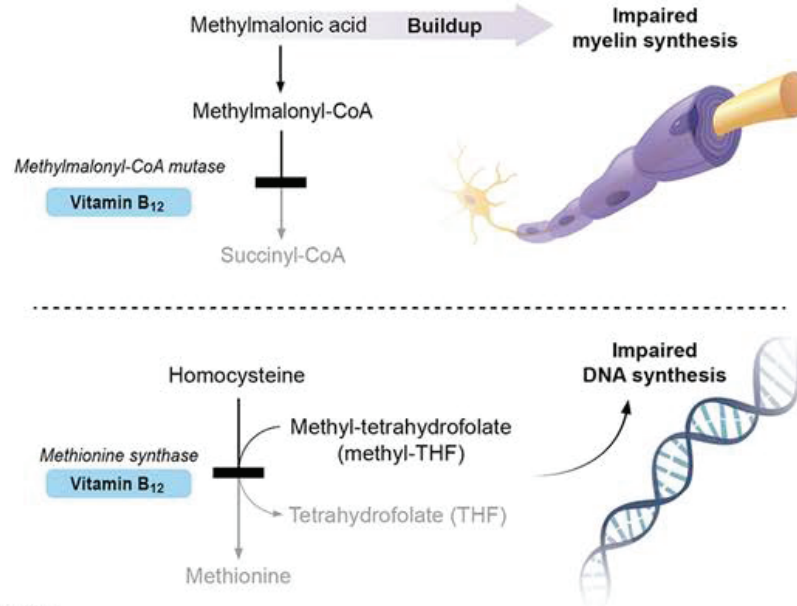
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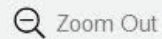
## Exhibit Display

Vitamin B<sub>12</sub> deficiency

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This patient has features of anemia (eg, exertional dyspnea, fatigue, pallor) with associated neurologic deficits that are highly suggestive of **vitamin B<sub>12</sub> deficiency**. The hematologic manifestations of B<sub>12</sub> deficiency (eg, **megaloblastic anemia**, pancytopenia) are related to impaired DNA synthesis.

Vitamin B<sub>12</sub> (hydroxocobalamin) also serves as a cofactor for methylmalonyl-CoA mutase (converts methylmalonyl-CoA to succinyl-CoA) and methionine synthase (converts homocysteine and folic acid to methionine). B<sub>12</sub> deficiency consequently results in **elevated** levels of **serum methylmalonic acid and homocysteine**. Increased methylmalonic acid levels can disrupt myelin synthesis and result in **subacute combined degeneration** of the dorsal columns (eg, loss of proprioception/vibration, Romberg sign) and lateral corticospinal tract (eg, spastic muscle weakness, hyperreflexia). Axonal degeneration of peripheral nerves can also be seen.

**(Choice A)** Glucose-6-phosphate dehydrogenase deficiency (G6PD) leads to acute hemolytic anemia in response to oxidative stress. Neurologic manifestations are not present in G6PD-associated anemia.

**(Choice B)** Erythrocyte glutathione reductase activity may be decreased in patients with vitamin B<sub>2</sub> (riboflavin) deficiency because glutathione reductase uses bound FAD (derived from vitamin B<sub>2</sub>) and NADPH as cofactors to reduce disulfide bonds. Vitamin B<sub>2</sub> deficiency typically presents with normocytic





response to oxidative stress. Neurologic manifestations are not present in G6PD-associated anemia.

**(Choice B)** Erythrocyte glutathione reductase activity may be decreased in patients with vitamin B<sub>2</sub> (riboflavin) deficiency because glutathione reductase uses bound FAD (derived from vitamin B<sub>2</sub>) and NADPH as cofactors to reduce disulfide bonds. Vitamin B<sub>2</sub> deficiency typically presents with normocytic anemia and inflammation of the lips (cheilosis), mouth (stomatitis), and/or tongue (glossitis).

**(Choice C)** Pyruvate kinase generates ATP through the conversion of phosphoenolpyruvate to pyruvate. Pyruvate kinase deficiency is an autosomal recessive condition that typically presents with congenital hemolytic anemia due to impaired glycolytic ATP generation.

**(Choice D)** Transketolase is an enzyme of the hexose monophosphate pathway that utilizes thiamine (vitamin B<sub>1</sub>) as a coenzyme. Erythrocyte transketolase activity is decreased in thiamine deficiency, which causes Wernicke-Korsakoff syndrome and beriberi.

**(Choice F)** Serum protoporphyrin levels are increased in iron deficiency anemia, lead poisoning, and erythropoietic protoporphyria. Lead poisoning can cause sideroblastic anemia and peripheral neuropathy, but other characteristic features (eg, abdominal/musculoskeletal pain, cognitive impairment, nephropathy) are not evident in this patient.



**(Choice C)** Pyruvate kinase generates ATP through the conversion of phosphoenolpyruvate to pyruvate.

Pyruvate kinase deficiency is an autosomal recessive condition that typically presents with congenital hemolytic anemia due to impaired glycolytic ATP generation.

**(Choice D)** Transketolase is an enzyme of the hexose monophosphate pathway that utilizes thiamine (vitamin B<sub>1</sub>) as a coenzyme. Erythrocyte transketolase activity is decreased in thiamine deficiency, which causes Wernicke-Korsakoff syndrome and beriberi.

**(Choice F)** Serum protoporphyrin levels are increased in iron deficiency anemia, lead poisoning, and erythropoietic protoporphyria. Lead poisoning can cause sideroblastic anemia and peripheral neuropathy, but other characteristic features (eg, abdominal/musculoskeletal pain, cognitive impairment, nephropathy) are not evident in this patient.

### **Educational objective:**

Vitamin B<sub>12</sub> deficiency often presents with megaloblastic anemia (impaired DNA synthesis) and neurologic deficits (impaired myelin synthesis). Characteristic neurologic findings include subacute combined degeneration of the dorsal columns and lateral corticospinal tract. Elevations in methylmalonic acid and homocysteine levels occur due to decreased metabolism of these molecules.

### **References**



A 55-year-old man comes to the office due to intermittent abdominal pain. He has no difficulty or pain with swallowing. The patient occasionally uses over-the-counter pain medicine for osteoarthritis of the right knee. He does not use alcohol or tobacco and has no history of cancer in the family. He works as an air traffic controller at a busy airport. Upper gastrointestinal endoscopy shows an ulcer in the distal duodenum. Fasting serum gastrin concentration is at the upper limit of normal and rises in response to intravenous secretin. This patient's condition is most likely caused by which of the following processes?

- ☐ A. Autoimmune destruction
- ☐ B. *Helicobacter pylori* infection
- ☐ C. Mucosal immune dysregulation
- ☐ D. Neoplasm
- ☐ E. Nonsteroidal anti-inflammatory drug use
- ☐ F. Stress

**Submit**

Block Time Remaining: 00:08:53

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Feedback



Suspend



End Block





A 55-year-old man comes to the office due to intermittent abdominal pain. He has no difficulty or pain with swallowing. The patient occasionally uses over-the-counter **pain medicine** for osteoarthritis of the right knee. He does not use alcohol or tobacco and has no history of cancer in the family. He works as an air traffic controller at a busy airport. Upper gastrointestinal endoscopy shows an **ulcer** in the distal duodenum. Fasting **serum gastrin** concentration is at the upper limit of normal and rises in response to intravenous **secretin**. This patient's condition is most likely caused by which of the following processes?

- ☐ A. Autoimmune destruction (2%)
- ☒ B. *Helicobacter pylori* infection (29%)
- ☐ C. Mucosal immune dysregulation (2%)
- ☒ D. Neoplasm (36%)
- ☐ E. Nonsteroidal anti-inflammatory drug use (22%)
- ☐ F. Stress (7%)





Item 14 of 40

Question Id: 305



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

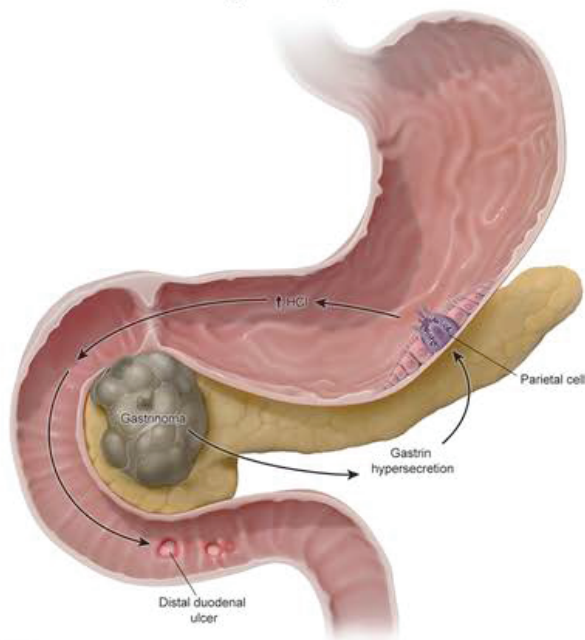
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### Exhibit Display

#### Zollinger-Ellison syndrome



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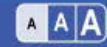
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This patient's distal duodenal ulcer and high-normal gastrin levels that rise in response to secretin administration are suggestive of **Zollinger-Ellison syndrome (ZES)**. This condition is caused by **gastrin-secreting tumors** (gastrinomas) that are often malignant and usually located in the small intestine or pancreas. Gastrin causes parietal cell hyperplasia and stimulates gastric acid secretion, resulting in the development of **peptic ulcers**, heartburn, and **diarrhea** (excess gastric acid impairs intestinal epithelial cells and digestive enzymes). Although most proximal duodenal ulcers are caused by *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug (NSAID) use (**Choice E**), ulcers found **beyond the duodenal bulb** suggest ZES.

**Secretin** is a hormone released from the duodenum in response to acid and fat in the small intestine. The hormone increases pancreatic bicarbonate secretion and inhibits the release of gastrin from normal gastric G cells. However, secretin paradoxically **stimulates gastrin release from gastrinomas** due to abnormal adenylate cyclase activation. As such, secretin administration can be used to differentiate ZES from other causes of hypergastrinemia (eg, atrophic gastritis).

**(Choice A)** Autoimmune gastritis (chronic atrophic gastritis) involves the body/fundus of the stomach with antral sparing. CD4<sup>+</sup> T cell-mediated parietal cell destruction causes impaired gastric acid and intrinsic







causes of hypergastrinemia (eg, atrophic gastritis).

**(Choice A)** Autoimmune gastritis (chronic atrophic gastritis) involves the body/fundus of the stomach with antral sparing. CD4<sup>+</sup> T cell-mediated parietal cell destruction causes impaired gastric acid and intrinsic factor secretion, resulting in achlorhydria and pernicious anemia, respectively. Low acid levels stimulate gastrin release from G cells (hypergastrinemia), but secretin administration causes a reduction in gastrin levels.

**(Choice B)** *H pylori* infection is associated with chronic antral-predominant gastritis, which may lead to a reduction in somatostatin-producing cells (delta cells). Lack of inhibition by somatostatin allows for excessive gastrin release, which promotes gastric acid hypersecretion and proximal duodenal ulcer formation. Secretin administration typically causes a reduction in gastrin levels in these patients.

**(Choice C)** Crohn disease is associated with dysregulation of the mucosal immune response, intestinal epithelial dysfunction, and altered composition of gut flora. Patients characteristically have linear ulcerations with adjacent normal-appearing mucosa (cobblestone appearance) in the small intestine.

**(Choice F)** Stress-related mucosal disease can occur with severe physiologic stress (eg, shock, head trauma, burns), but the association between psychological stress (eg, working as an air traffic controller) and peptic ulcer formation is controversial. Nonetheless, neither form of stress would cause distal



ulcerations with adjacent normal-appearing mucosa (cobblestone appearance) in the small intestine.

**(Choice F)** Stress-related mucosal disease can occur with severe physiologic stress (eg, shock, head trauma, burns), but the association between psychological stress (eg, working as an air traffic controller) and peptic ulcer formation is controversial. Nonetheless, neither form of stress would cause distal duodenal ulcers and hypergastrinemia.

### Educational objective:

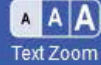
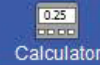
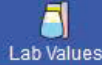
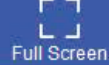
Zollinger-Ellison syndrome is caused by gastrinomas located in the small intestine/pancreas and presents with peptic ulcers (especially distal duodenal ulcers), heartburn, and diarrhea. Patients typically have elevated gastrin levels that rise in response to exogenous secretin administration. In contrast, secretin inhibits release of gastrin from normal gastric G cells.

### References

- [Hypergastrinemia.](#)

Pathology	Gastrointestinal & Nutrition	Zollinger ellison syndrome
Subject	System	Topic

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A 65-year-old man is evaluated in the clinic due to several months of abdominal pain and vomiting. The pain starts 2 to 3 hours after meals, is characterized as crampy, and is often associated with bilious vomiting. Lately, the patient has been tolerating only liquids and has consequently lost 12 lbs in the past 4 months. On physical examination, he has mild epigastric tenderness on deep palpation. Contrast-enhanced CT scan of the abdomen shows an irregular mass in the third portion of the duodenum that is infiltrating beyond the gut wall. If this mass continues to enlarge, which of the following structures is most likely to be compromised in this patient?

- ☐ A. Common bile duct
- ☐ B. Gastroduodenal artery
- ☐ C. Portal vein
- ☐ D. Superior mesenteric artery
- ☐ E. Ureter

**Submit**

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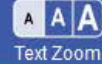
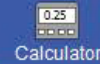
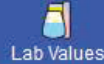
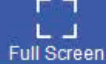
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Feedback

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A 65-year-old man is evaluated in the clinic due to several months of abdominal pain and vomiting. The pain starts 2 to 3 hours after meals, is characterized as crampy, and is often associated with **bilious vomiting**. Lately, the patient has been tolerating only liquids and has consequently lost 12 lbs in the past 4 months. On physical examination, he has mild epigastric tenderness on deep palpation. Contrast-enhanced CT scan of the abdomen shows an irregular mass in the third portion of the duodenum that is infiltrating beyond the gut wall. If this mass continues to enlarge, which of the following structures is most likely to be compromised in this patient?

- ☐ A. Common bile duct (12%)
- ☐ B. Gastroduodenal artery (18%)
- ☐ C. Portal vein (6%)
- ☒ D. Superior mesenteric artery (58%)
- ☐ E. Ureter (3%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



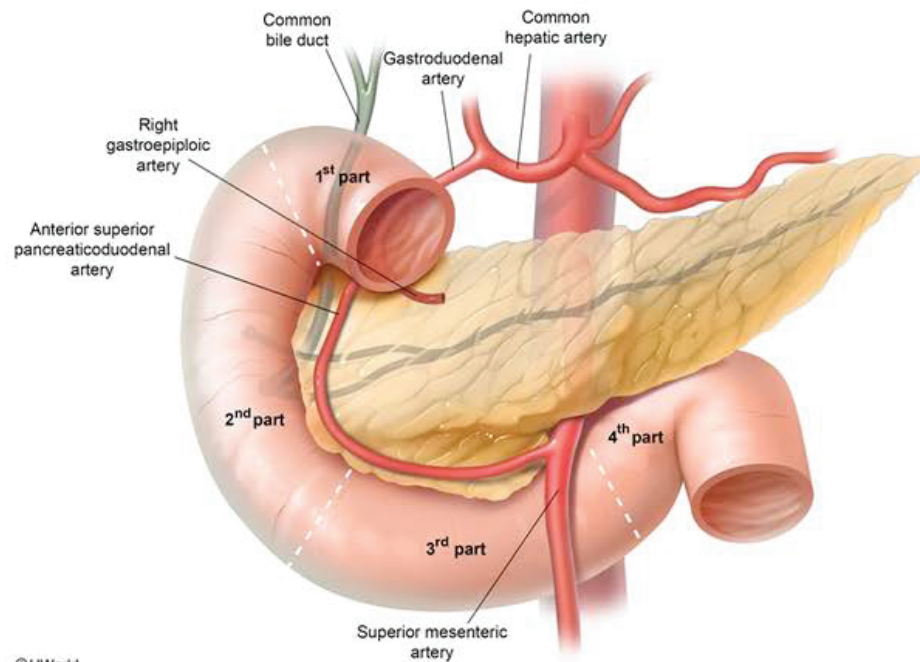
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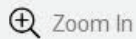
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## Exhibit Display

## Duodenum segments



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Zoom In



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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Superior mesenteric  
artery

The first part of the duodenum emerges from the pylorus of the stomach and is horizontally oriented over the first lumbar vertebra. It is the only part of the duodenum that is not retroperitoneal. The second part of the duodenum courses inferiorly from the level of L1 to L3. This part of the duodenum is in close relation to the head of the pancreas and contains the ampulla of Vater, the site where pancreatic and common bile duct secretions are released.

The **third part** of the **duodenum** courses horizontally over L3, the abdominal aorta, and the inferior vena cava. It is in close association with the uncinate process of the pancreas and the **superior mesenteric artery** and vein. Small bowel malignancies are rare; if they occur in the third part of the duodenum, anterior tumor invasion could compromise the superior mesenteric vessels. The fourth part of the duodenum courses superiorly and to the left of the L2 and L3 vertebrae and becomes the jejunum past the ligament of Treitz.

**(Choice A)** The common bile duct is formed when the common hepatic duct and cystic duct join in the porta hepatis region of the hepatoduodenal ligament. The common bile duct courses inferiorly, posterior to the first part of the duodenum and within the head of the pancreas, to drain into the second part of the duodenum.



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Next



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Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

duodenum.

**(Choice B)** The gastroduodenal artery arises from the common hepatic artery and courses inferiorly, posterior to the first part of the duodenum, where it then splits into the anterior superior pancreaticoduodenal artery and the right gastroepiploic artery. Peptic ulcers involving the posterior duodenal bulb can erode into the gastroduodenal artery and cause bleeding.

**(Choice C)** The portal vein is formed by the union of the superior mesenteric and splenic veins in the retroperitoneum. It is located posterior to the pancreas at the level of the first lumbar vertebra and makes no contact with the duodenum.

**(Choice E)** The left ureter has no relation to the duodenum. The right ureter courses retroperitoneally, posterior to the second part of the duodenum, for a short length.

### Educational objective:

The third part of the duodenum courses horizontally across the abdominal aorta and inferior vena cava at the level of the third lumbar vertebra. The superior mesenteric vessels lie anterior to the duodenum at this location.

### References

- [Upper gastrointestinal bleeding due to superior mesenteric artery to duodenum fistula: rare complication](#)



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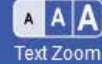
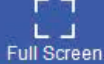
Feedback



Suspend



End Block



A 32-year-old man comes to the office due to a substernal burning sensation that has been occurring intermittently over the last 6 months. The sensation worsens with spicy and fatty meals and is associated with food regurgitation and a sour taste in the back of the throat. He has no projectile vomiting, dysphagia, or unexpected weight loss. Medical history is significant for cystic fibrosis complicated by pancreatic insufficiency, for which the patient takes pancreatic enzyme replacement therapy with all meals. Vital signs are within normal limits. The abdomen is soft and nontender. He is prescribed omeprazole with subsequent improvement in his gastroesophageal reflux symptoms. In this patient, absorption of which of the following nutrients will likely improve due to initiation of this new medication?

- ☐ A. Amino acids
- ☐ B. Calcium
- ☐ C. Dietary fat
- ☐ D. Iron
- ☐ E. Magnesium





intermittently over the last 6 months. The sensation worsens with spicy and fatty meals and is associated with food regurgitation and a sour taste in the back of the throat. He has no projectile vomiting, dysphagia, or unexpected weight loss. Medical history is significant for cystic fibrosis complicated by pancreatic insufficiency, for which the patient takes pancreatic enzyme replacement therapy with all meals. Vital signs are within normal limits. The abdomen is soft and nontender. He is prescribed omeprazole with subsequent improvement in his gastroesophageal reflux symptoms. In this patient, absorption of which of the following nutrients will likely improve due to initiation of this new medication?

- ☐ A. Amino acids (22%)
- ☐ B. Calcium (13%)
- ☒ C. Dietary fat (35%)
- ☐ D. Iron (19%)
- ☐ E. Magnesium (8%)

Correct

35%

13 secs

12/27/2020

Block Time Remaining: 00:11:40

TUTOR

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Feedback

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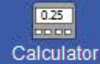
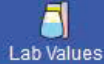
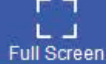


## Proton pump inhibitors

<b>Mechanism of action</b>	<ul style="list-style-type: none"> <li>Irreversible inhibition of parietal cell hydrogen-potassium-ATPase</li> </ul>
<b>Common uses</b>	<ul style="list-style-type: none"> <li>Gastroesophageal reflux disease</li> <li>Peptic ulcer disease</li> </ul>
<b>Adverse effects</b>	<ul style="list-style-type: none"> <li>Malabsorption of calcium, iron, magnesium &amp; vitamin B<sub>12</sub> <ul style="list-style-type: none"> <li>Enhances fat absorption in patients given pancreatic enzyme replacement therapy</li> </ul> </li> <li>Increases risk of infection (eg, <i>Clostridioides</i> [formerly <i>Clostridium</i>] <i>difficile</i>, pneumonia)</li> <li>Osteoporosis, chronic kidney disease, SIBO</li> </ul>

**SIBO** = small intestinal bacterial overgrowth.

This patient with heartburn and regurgitation has the classic manifestations of gastroesophageal reflux disease, a common disorder that occurs when gastric acid refluxes into the esophagus. The mainstay of therapy is gastric acid suppression, usually with proton pump inhibitors (PPIs) (eg, pantoprazole).



This patient with heartburn and regurgitation has the classic manifestations of gastroesophageal reflux disease, a common disorder that occurs when gastric acid refluxes into the esophagus. The mainstay of therapy is gastric acid suppression, usually with **proton pump inhibitors** (PPIs) (eg, pantoprazole, omeprazole).

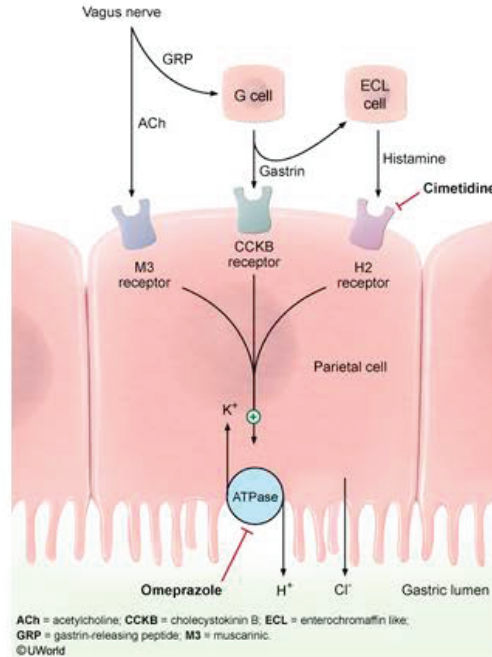
PPIs irreversibly inhibit the **hydrogen-potassium-ATPase pump** found in parietal cells, thereby inhibiting hydrochloric acid secretion into the stomach lumen. Although this effectively raises the stomach pH and prevents gastric acid irritation of the esophagus, the acidic environment of the stomach is necessary to absorb certain nutrients. Therefore, common adverse effects of PPIs include malabsorption of calcium, iron, magnesium, and vitamin B<sub>12</sub> (**Choices B, D, and E**).

Patients with **pancreatic insufficiency** (eg, cystic fibrosis, chronic pancreatitis) cannot synthesize the pancreatic enzymes required for digestion of protein, fat, and carbohydrates. As such, the condition is managed with pancreatic enzyme replacements, which contain varying amounts of lipase, amylase, and protease. Unlike amylase and protease, which are activated by the low pH of the stomach, **lipase**, which plays a vital role in fat digestion, is **inactivated by the acidic environment** of the stomach. Therefore, by decreasing gastric hydrochloric acid production, **PPI use increases lipase activity** (ie, it prevents exogenous lipase from being denatured as it passes through the stomach), **enhancing fat absorption** in



### Exhibit Display

#### Parietal cell acid secretion



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Reset

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

exogenous lipase from being denatured as it passes through the stomach), enhancing fat absorption in patients dependent on pancreatic enzyme replacement therapy.

**(Choice A)** Protein digestion of amino acids requires the activity of a protease known as pepsin, which is more active at low pH. Although one might expect the elevated stomach pH to inhibit protein absorption, chronic PPI use has not been associated with protein malabsorption (likely due to functional overlap with pancreatic and enteric proteases).

### Educational objective:

Proton pump inhibitors (PPI) prevent the hydrogen-potassium-ATPase pump found in parietal cells from releasing hydrochloric acid into the stomach lumen. Chronic PPI use protects exogenously administered lipase and enhances fat absorption in patients dependent on pancreatic enzyme replacement therapy.

### References

- Optimising the therapy of exocrine pancreatic insufficiency by the association of a proton pump inhibitor to enteric coated pancreatic extracts.
- Proton pump inhibitors and risk of vitamin and mineral deficiency: evidence and clinical implications.

Pharmacology

Gastrointestinal &amp; Nutrition

Proton pump inhibitors

Subject

System

Topic

Block Time Remaining: 00:11:40

TUTOR

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Feedback

Suspend

End Block

A 67-year-old man comes to the emergency department due to progressive fever and lethargy. The patient has also had severe right shoulder and abdominal pain, nausea, and vomiting for the past 2 days. He had an appendectomy during childhood and a pacemaker placed 10 years ago for symptomatic sinus bradycardia. He has no other medical problems and takes no medications. The patient does not use tobacco but drinks an occasional beer. Temperature is 38.4 C (101.1 F), blood pressure is 80/50 mm Hg, and pulse is 120/min and regular. Abdominal examination shows generalized tenderness with rebound tenderness. Right shoulder examination is normal. Upright chest x-ray is shown below.

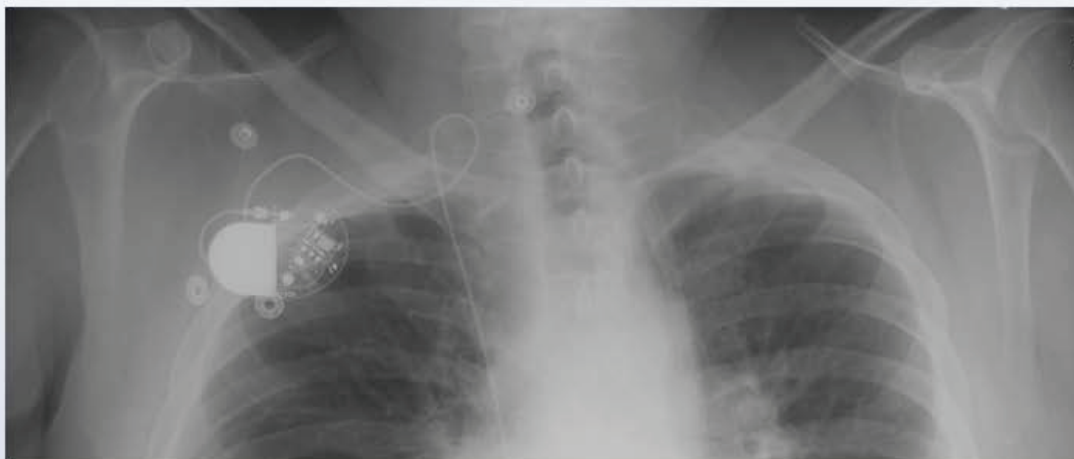
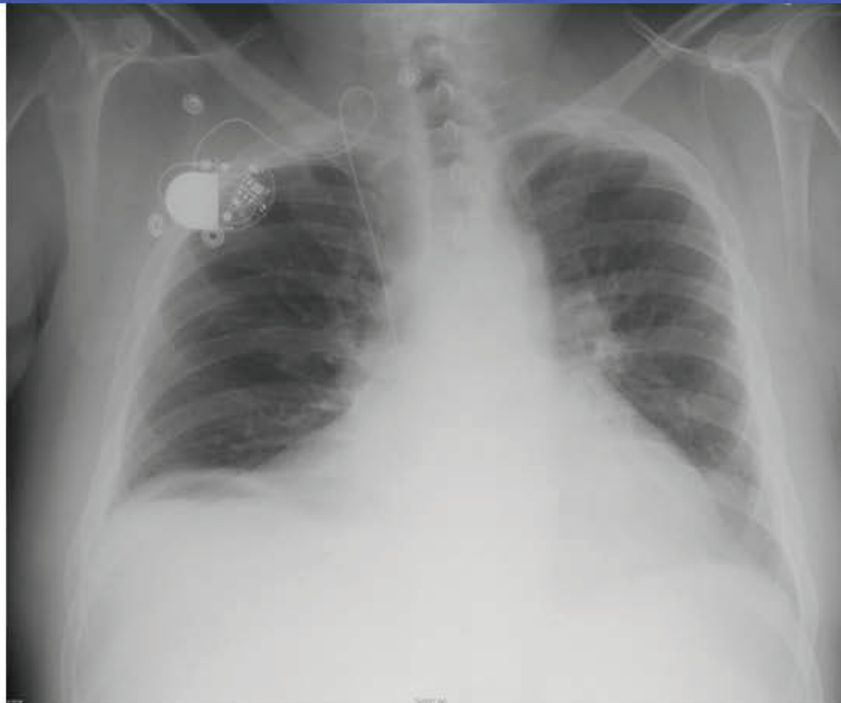


Exhibit Display



Zoom In Zoom Out Reset New Existing My Notebook

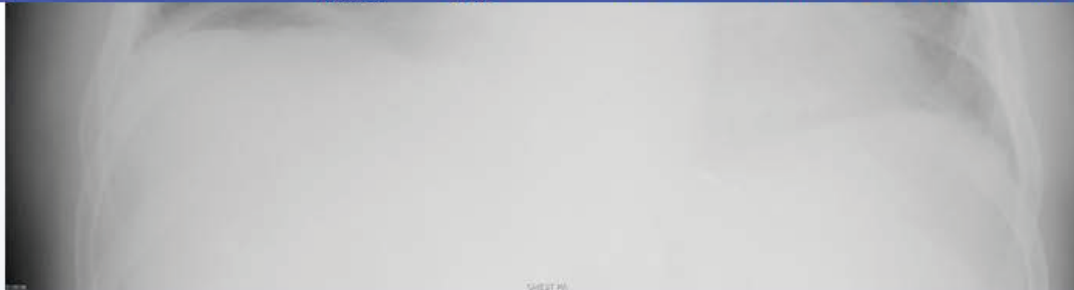




Which of the following is the most likely cause of this patient's condition?

- ☐ A. Acute cholecystitis
- ☐ B. Acute pancreatitis
- ☐ C. Nephrolithiasis
- ☐ D. Perforated viscus
- ☐ E. Small bowel obstruction

Submit



Which of the following is the most likely cause of this patient's condition?

- ☐ A. Acute cholecystitis (24%)
- ☐ B. Acute pancreatitis (13%)
- ☐ C. Nephrolithiasis (0%)
- ☒ D. Perforated viscus (57%)
- ☐ E. Small bowel obstruction (4%)

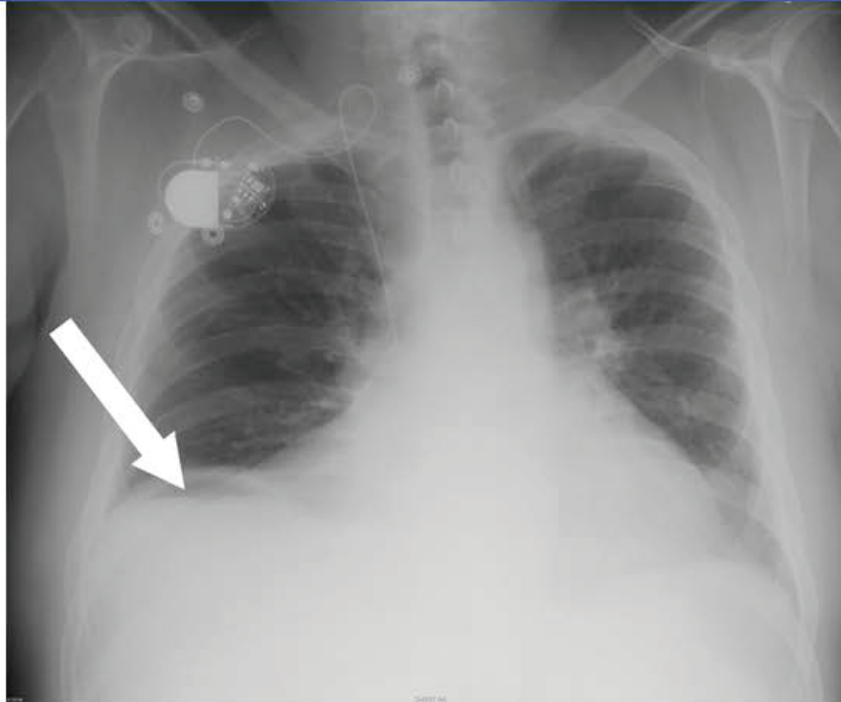
Correct

57%  
Answered correctly

54 secs  
Time spent

02/13/2021  
Last updated

Exhibit Display



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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Settings

This patient's upright chest x-ray demonstrates **free air** under the diaphragm (**pneumoperitoneum**), likely due to **perforation** of a hollow abdominal viscus. The most common cause of pneumoperitoneum is a perforated duodenal ulcer, but perforation can occur anywhere along the gastrointestinal (or female reproductive) tract due to ulcers, tumors, trauma, or iatrogenic causes (eg, endoscopy, surgery).

Contamination of the sterile peritoneal cavity with bowel contents leads to chemical (acid or chyme-related) or bacterial **peritonitis**, which, if left untreated, can progress to sepsis and death. Diffuse irritation of the parietal peritoneum results in severe abdominal pain with **rigidity** and **rebound tenderness**. **Shoulder pain** is another frequent finding and reflects referred pain from diaphragmatic irritation. Referred pain is due to convergence of multiple nociceptors (visceral and somatic) onto a single secondary neuron within the spinal cord, which causes the brain to misinterpret visceral pain as arising from a body surface.

**(Choice A)** Other common causes of abdominal pain with associated diaphragmatic irritation and referred shoulder pain include acute cholecystitis/biliary colic and splenic lacerations. However, these would not be associated with intraabdominal free air.

**(Choice B)** Acute pancreatitis causes epigastric abdominal pain that may be referred to the back. X-ray findings are often normal, although a localized ileus near the inflamed pancreas (sentinel loop sign) may be seen.



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**(Choice B)** Acute pancreatitis causes epigastric abdominal pain that may be referred to the back. X-ray findings are often normal, although a localized ileus near the inflamed pancreas (sentinel loop sign) may be seen.

**(Choice C)** **Nephrolithiasis** typically presents with colicky flank pain that is referred to the groin. Radiopaque stones (calcium, struvite, and cystine) may be visualized on plain radiography.

**(Choice E)** **Small bowel obstruction** causes poorly localized, constant abdominal pain, which can be referred to the epigastrium. Plain radiography demonstrates dilation of the small bowel with air fluid levels; free air is not seen in the absence of perforation.

### Educational objective:

Pneumoperitoneum is air or gas in the peritoneal cavity; it can be seen as free air under the diaphragm in an upright chest x-ray. The most common cause is a perforated duodenal ulcer, but perforation can occur anywhere along the gastrointestinal (or female reproductive) tract. Subsequent peritonitis can lead to diffuse abdominal pain with rebound and guarding, sometimes with referred shoulder pain due to diaphragmatic irritation.

Anatomy

Gastrointestinal &amp; Nutrition

Perforated viscus

Subject

System

Topic

Block Time Remaining: 00:12:34

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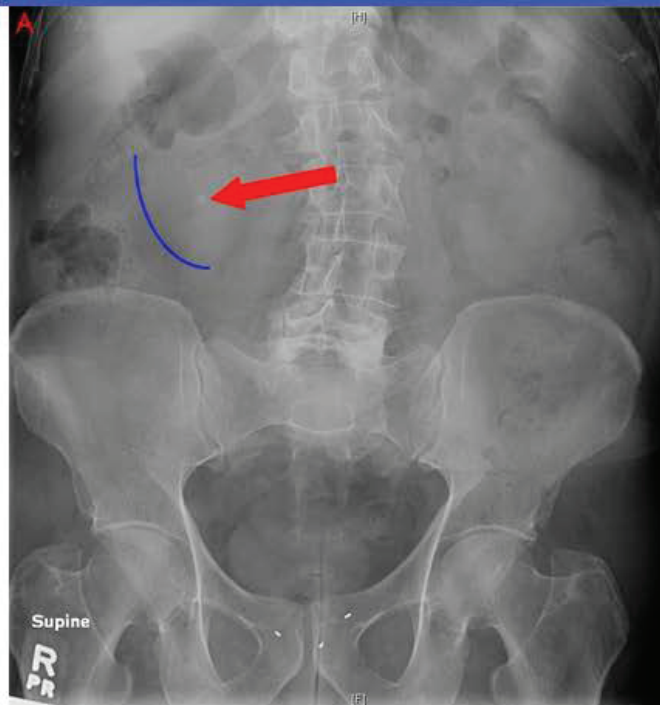
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(Choice B) Acute pancreatitis causes epigastric abdominal pain that may be referred to the back. X ray

Exhibit Display



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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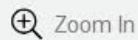
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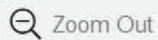
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(Choice B) Acute pancreatitis causes epigastric abdominal pain that may be referred to the back. X ray

## Exhibit Display



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My Notebook

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Subject

System

Topic

Block Time Remaining: 00:12:34

TUTOR

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Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

A 23-year-old-man is brought to the emergency department after he was stabbed in the right upper quadrant of the abdomen. His blood pressure is 70/42 mm Hg, pulse is 135/min, and respirations are 26/min; pulse oximetry shows oxygen saturation of 95% on room air. Physical examination shows a stab wound 2 cm inferior to the right costal margin. The patient's abdomen is firm and distended. Focused assessment with sonography for trauma (FAST) is positive for blood in the right upper quadrant. He is taken for immediate laparotomy, and approximately 1 liter of blood is evacuated from the peritoneal cavity. Brisk, nonpulsatile bleeding is seen emanating from behind the liver. The surgeon occludes the hepatoduodenal ligament, but the patient continues to hemorrhage. Which of the following structures is the most likely source of this patient's bleeding?

- ☐ A. Common bile duct
- ☐ B. Cystic artery
- ☐ C. Hepatic artery
- ☐ D. Inferior vena cava
- ☐ E. Portal vein



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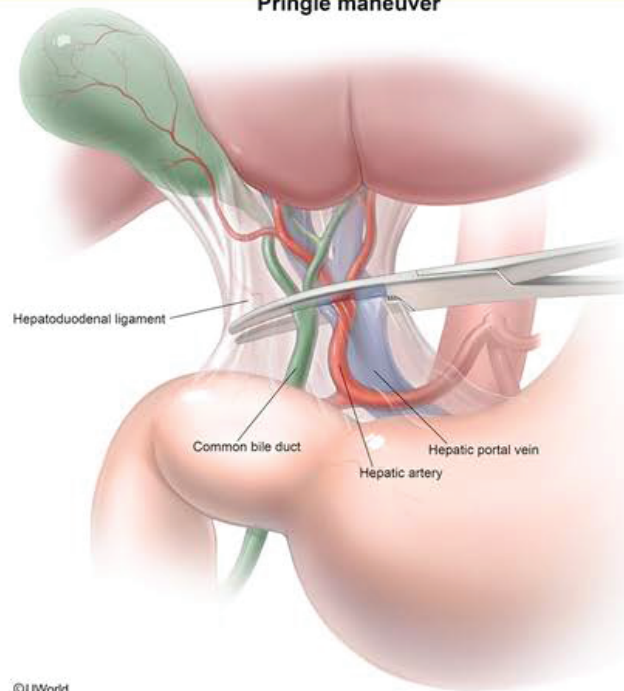
quadrant of the abdomen. His blood pressure is 70/42 mm Hg, pulse is 135/min, and respirations are 26/min; pulse oximetry shows oxygen saturation of 95% on room air. Physical examination shows a stab wound 2 cm inferior to the right costal margin. The patient's abdomen is firm and distended. Focused assessment with sonography for trauma (FAST) is positive for blood in the right upper quadrant. He is taken for immediate laparotomy, and approximately 1 liter of blood is evacuated from the peritoneal cavity. Brisk, nonpulsatile bleeding is seen emanating from behind the liver. The surgeon occludes the hepatoduodenal ligament, but the patient continues to hemorrhage. Which of the following structures is the most likely source of this patient's bleeding?

- ☐ A. Common bile duct (0%)
- ☐ B. Cystic artery (9%)
- ☐ C. Hepatic artery (6%)
- ☒ D. Inferior vena cava (65%)
- ☐ E. Portal vein (17%)



### Exhibit Display

#### Pringle maneuver



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New | Existing

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The **portal triad** runs through the **hepatoduodenal ligament** and is composed of the hepatic artery, portal vein, and common bile duct. In the setting of traumatic liver injury with persistent bleeding, **occlusion** of the hepatoduodenal ligament can be performed to identify the vascular source (ie, the Pringle maneuver). If liver **bleeding does not cease** when the portal triad is occluded, it is likely that there has been injury to the **inferior vena cava** or hepatic veins. Although the inferior vena cava is a retroperitoneal structure, penetrating trauma can disrupt tissue barriers, facilitating bleeding into the peritoneal compartment.

**(Choice A)** The common bile duct makes up one-third of the portal triad. Damage to the biliary ducts can cause biliary leakage and bile peritonitis.

**(Choice B)** The cystic artery most commonly arises from the right hepatic artery and would be devascularized following portal triad occlusion. In addition, arterial bleeding is usually pulsatile whereas venous bleeding is nonpulsatile.

**(Choices C and E)** The hepatic artery and portal vein are part of the portal triad; occlusion of the hepatoduodenal ligament would cause the bleeding to stop if either of these vessels is the source.

### Educational objective:

Occlusion of the portal triad can be used to distinguish the source of right upper quadrant bleeding. If the



cause biliary leakage and bile peritonitis.

**(Choice B)** The cystic artery most commonly arises from the right hepatic artery and would be devascularized following portal triad occlusion. In addition, arterial bleeding is usually pulsatile whereas venous bleeding is nonpulsatile.

**(Choices C and E)** The hepatic artery and portal vein are part of the portal triad; occlusion of the hepatoduodenal ligament would cause the bleeding to stop if either of these vessels is the source.

### Educational objective:

Occlusion of the portal triad can be used to distinguish the source of right upper quadrant bleeding. If the bleeding subsides following occlusion, the source is likely to be the hepatic artery or portal vein. If hepatic bleeding persists after occlusion, the inferior vena cava or hepatic veins are likely to be injured.

### References

- [Vascular control during hepatectomy: review of methods and results.](#)
- [Emergency strategies and trends in the management of liver trauma.](#)

Anatomy

Gastrointestinal &amp; Nutrition

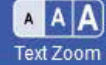
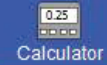
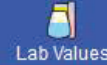
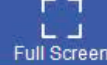
Penetrating abdominal trauma

Subject

System

Topic





A 14-month-old girl is brought to the office due to a 2-month history of diarrhea. Her parents report that she has 3-5 loose, nonbloody bowel movements daily with occasional episodes of vomiting. She was breastfed exclusively until age 9 months and has since had a well-varied diet including whole milk, fruits, vegetables, bread, and meats. However, the girl has been less interested in food over the past several weeks. There is no history of travel or contacts with similar symptoms. On physical examination, the patient appears well but has lost 1.1 kg (2.5 lb) in the last 2 months. After laboratory evaluation, duodenal biopsy findings are shown in the [exhibit](#). Which of the following would most likely improve this patient's symptoms?

- ☐ A. Acid reduction therapy
- ☐ B. Anti-inflammatory medications
- ☐ C. Antibiotic therapy
- ☐ D. Enzyme supplementation
- ☐ E. Modified dairy diet
- ☐ F. Modified grain diet





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Previous



Next



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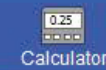
Tutorial



Lab Values



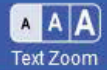
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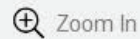
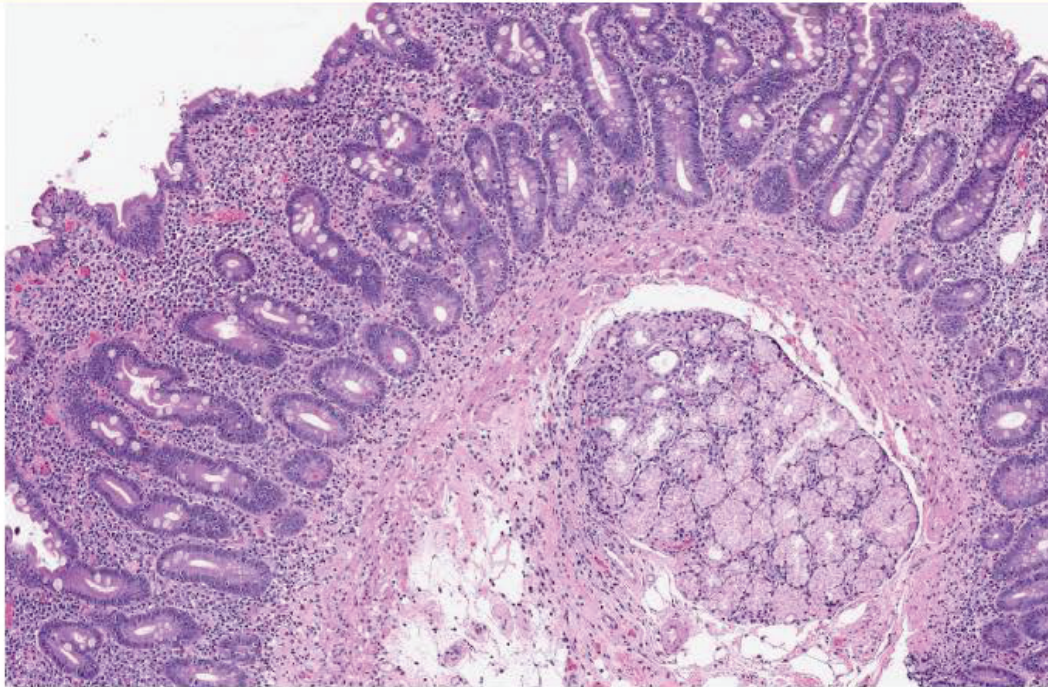


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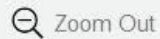


Settings

Exhibit Display



Zoom In



Zoom Out



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My Notebook



2



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

has 3-5 loose, nonbloody bowel movements daily with occasional episodes of vomiting. She was breastfed exclusively until age 9 months and has since had a well-varied diet including whole milk, fruits, vegetables, bread, and meats. However, the girl has been less interested in food over the past several weeks. There is no history of travel or contacts with similar symptoms. On physical examination, the patient appears well but has lost 1.1 kg (2.5 lb) in the last 2 months. After laboratory evaluation, duodenal biopsy findings are shown in the [exhibit](#). Which of the following would most likely improve this patient's symptoms?

- ☐ A. Acid reduction therapy (2%)
- ☐ B. Anti-inflammatory medications (7%)
- ☐ C. Antibiotic therapy (3%)
- ☐ D. Enzyme supplementation (3%)
- ☐ E. Modified dairy diet (8%)
- ☒ F. Modified grain diet (74%)

Correct

74%



01 min, 27 secs



02/03/2021

Block Time Remaining: 00:14:17

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2



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



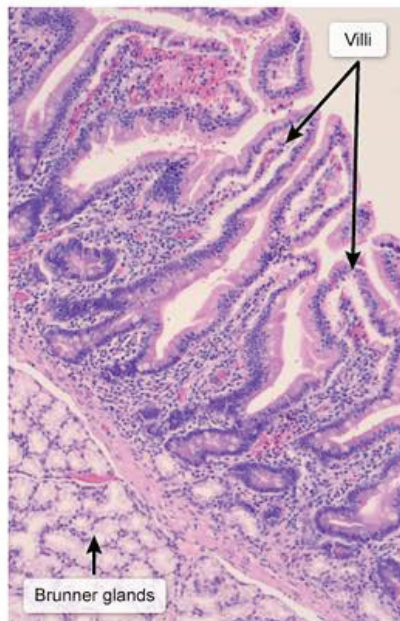
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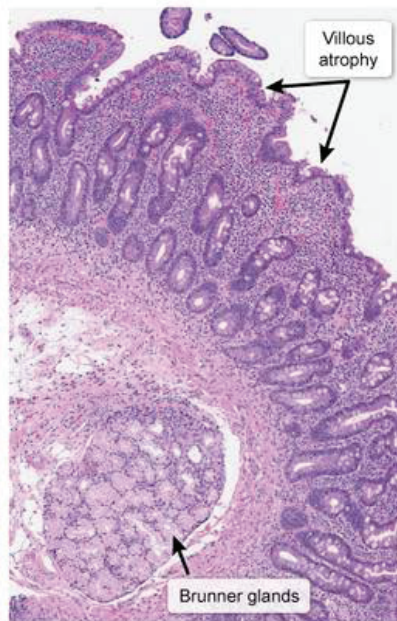
## Exhibit Display

Normal duodenum

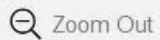


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Celiac disease



Zoom In



Zoom Out



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New



Existing



My Notebook



My Notebook



2



Feedback



Suspend



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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**Celiac disease** is a chronic malabsorptive disorder caused by a **hypersensitivity to gluten**, a protein found in wheat, barley, and rye. Gliadin (a gluten component) triggers an immune-mediated reaction causing **villous atrophy**, **crypt hyperplasia**, and **intraepithelial lymphocyte infiltration**. Normal intestinal villi allow for increased small intestinal surface area to begin the process of digestion and nutrient absorption. The atrophy in celiac disease causes impairment of nutrient absorption in the duodenum and proximal jejunum, regions where the concentration of gluten is the highest.

Classic celiac disease presents after introduction of gluten into the diet (between age 6-24 months) with symptoms of malabsorption (eg, diarrhea, steatorrhea, flatulence, nutrient deficiencies, weight loss). Other manifestations include delayed puberty and short stature in children and anemia in adults. Screening is with serology testing for elevated IgA anti-endomysial and **anti-tissue transglutaminase antibodies**; diagnosis is confirmed by endoscopic biopsy. With strict adherence to a **gluten-free diet**, symptom resolution occurs within weeks and is followed by normalization of histology and antibody levels.

**(Choice A)** Mild gastroesophageal reflux is physiologic in healthy infants, but it can lead to irritability, poor feeding, and inadequate weight gain when severe. The diagnosis is often made clinically and can be treated with conservative changes (eg, smaller feedings) and acid suppression (eg, proton pump inhibitor). Refractory cases may require biopsy, which shows esophageal inflammation.



2



Feedback



Suspend



End Block



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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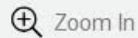
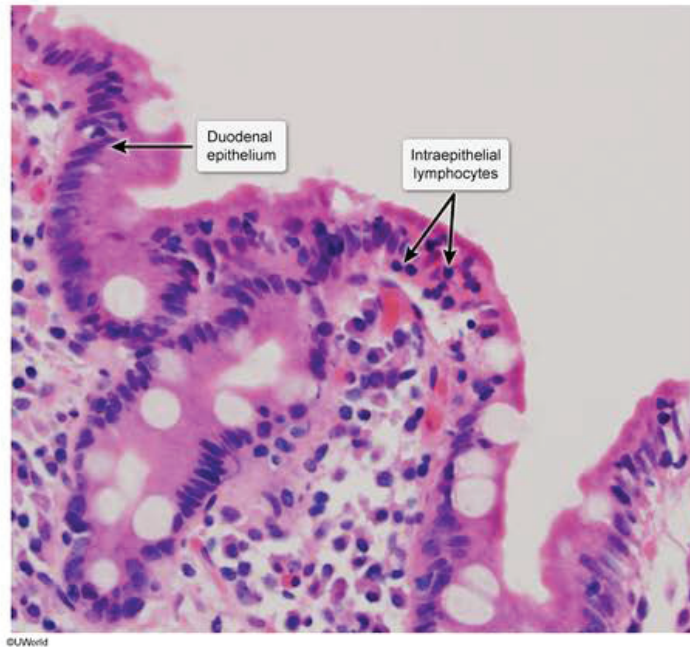


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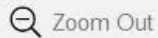
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## Exhibit Display

## Celiac disease



Zoom In



Zoom Out



Reset



New



Existing



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Refractory cases may require biopsy, which shows esophageal inflammation.

Block Time Remaining: 00:14:17

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2



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

feeding, and inadequate weight gain when severe. The diagnosis is often made clinically and can be treated with conservative changes (eg, smaller feedings) and acid suppression (eg, proton pump inhibitor). Refractory cases may require biopsy, which shows esophageal inflammation.

**(Choice B)** Anti-inflammatory medications (eg, glucocorticoids, aminosalicylates) are the mainstay of treatment for inflammatory bowel disease (ulcerative colitis [UC] and Crohn disease [CD]). Symptoms include abdominal pain, bloody diarrhea, and weight loss. Colonoscopy may show diffuse colonic inflammation in UC and focal areas of small intestinal and colonic inflammation in CD.

**(Choice C)** Tropical sprue can occur with extended travel to the tropics and presents with chronic diarrhea, abdominal pain, and flatulence along with similar histologic findings to celiac disease (eg, villous atrophy). The etiology is likely infectious, and the disease is treated with antibiotics. However, this patient has no history of travel.

**(Choices D and E)** Lactase supplementation or limited lactose intake is recommended for patients with lactose intolerance, which classically presents in older children and adults with bloating, flatulence, abdominal discomfort, and diarrhea. Although biopsy is not indicated for diagnosis, histology would show normal small intestinal architecture with decreased lactase activity.

**Educational objective:**



2



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

inflammation in UC and focal areas of small intestinal and colonic inflammation in CD.

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### Educational objective:

Celiac disease (gluten-sensitive enteropathy) classically presents between age 6-24 months with abdominal pain, diarrhea, vomiting, and weight loss. Duodenal biopsy reveals crypt hyperplasia, villous atrophy, and intraepithelial lymphocyte infiltration. Treatment with a gluten-free diet resolves symptoms and normalizes serology and histology.

Histology

Gastrointestinal &amp; Nutrition

Celiac disease



2



Feedback



Suspend



End Block



A 26-year-old woman comes to the office due to recurrent nausea and vomiting for the past several months. The patient experiences nausea and epigastric discomfort after meals and often feels full after eating only a small portion of food. On several occasions, she has had emesis containing particles of food that she ate several hours earlier. The patient has a 15-year history of type 1 diabetes mellitus complicated by diabetic nephropathy. Her medications include a basal-bolus insulin regimen and lisinopril. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. The abdomen is soft and nontender with no organomegaly. Bowel sounds are normal. Testing of stool for occult blood is negative. An upper gastrointestinal endoscopy is unremarkable. Which of the following mechanisms is most likely responsible for this patient's current symptoms?

- ☐ A. Decreased activity of vagus motor nucleus
- ☐ B. Disruption of lower esophageal sphincter
- ☐ C. Dysfunction of gastric enteric neurons
- ☐ D. Excessive production of cholecystikinin
- ☐ E. Hypertrophy of pyloric smooth muscles







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

months. The patient experiences nausea and epigastric discomfort after meals and often feels full after eating only a small portion of food. On several occasions, she has had emesis containing particles of food that she ate several hours earlier. The patient has a 15-year history of type 1 diabetes mellitus complicated by diabetic nephropathy. Her medications include a basal-bolus insulin regimen and lisinopril. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. The abdomen is soft and nontender with no organomegaly. Bowel sounds are normal. Testing of stool for occult blood is negative. An upper gastrointestinal endoscopy is unremarkable. Which of the following mechanisms is most likely responsible for this patient's current symptoms?

- ☐ A. ~~Decreased activity of vagus motor nucleus (15%)~~
- ☐ B. ~~Disruption of lower esophageal sphincter (11%)~~
- ☒ C. Dysfunction of gastric enteric neurons (63%)
- ☐ D. ~~Excessive production of cholecystokinin (3%)~~
- ☐ E. ~~Hypertrophy of pyloric smooth muscles (6%)~~





Diabetic gastroparesis	
Pathogenesis	<ul style="list-style-type: none"><li>• Autonomic neuropathy</li><li>• Destruction of enteric neurons</li><li>• Failure of relaxation in fundus &amp; uncoordinated peristalsis</li></ul>
Risk factors	<ul style="list-style-type: none"><li>• Long-standing diabetes (especially type 1)</li><li>• Chronic poor control</li><li>• Labile blood glucose</li></ul>
Clinical presentation	<ul style="list-style-type: none"><li>• Postprandial bloating &amp; vomiting</li><li>• Early satiety</li><li>• Impaired nutrition &amp; weight loss</li></ul>
Diagnosis	<ul style="list-style-type: none"><li>• Nuclear gastric emptying study: delayed transit into duodenum</li></ul>
Treatment	<ul style="list-style-type: none"><li>• Proton pump inhibitors: metoclopramide, erythromycin</li></ul>

This patient with diabetes has postprandial nausea, vomiting, early satiety, and regurgitation of undigested food particles, which is suggestive of **diabetic gastroparesis**. Gastroparesis is a type of **autonomic**





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## Treatment

- Promotility drugs: metoclopramide, erythromycin

This patient with diabetes has postprandial nausea, vomiting, early satiety, and regurgitation of undigested food particles, which is suggestive of **diabetic gastroparesis**. Gastroparesis is a type of **autonomic neuropathy** involving the gastrointestinal tract and is characterized by delayed gastric emptying not due to an obstruction.

Normal postprandial gastric activity is a multistep process that occurs in response to food ingestion. After food passes down the esophagus, vagally stimulated enteric neurons release nitric oxide to induce relaxation of the fundus of the stomach and accommodate the incoming food bolus. Specialized gastric pacemaker cells (interstitial cells of Cajal) initiate pacemaker potentials (slow waves), which generate circumferential contractions of the gastric smooth muscle (peristalsis). Peristalsis facilitates food mixing and propulsion toward the pylorus.

**Chronic hyperglycemia** in patients with diabetes can result in **destruction of the enteric neurons**. Loss of nitric oxide-containing neurons results in impaired fundal relaxation, and loss of the interstitial cells of Cajal results in uncoordinated smooth muscle contractions and ineffective peristalsis, both of which **delay gastric emptying**.

**(Choice A)** Chronic hyperglycemia can cause vagus nerve denervation with axonal damage, which can





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**gastric emptying.**

**(Choice A)** Chronic hyperglycemia can cause vagus nerve denervation with axonal damage, which can contribute to diabetic gastroparesis. However, the vagal motor nucleus is located in the brainstem and is typically unaffected by diabetes.

**(Choice B)** Disruption of the lower esophageal sphincter can cause symptoms of acid reflux. Although severe gastroesophageal reflux can cause regurgitation, a history of heartburn or epigastric pain would be expected. In addition, upper endoscopy typically shows evidence of esophagitis (eg, mucosal erythema, exudates).

**(Choice D)** Cholecystokinin is secreted in response to fat- or protein-rich meals and slows gastric emptying to improve digestion of these nutrients. Cholecystokinin secretion may actually be reduced in diabetes and is not thought to be a major cause of diabetic gastroparesis.

**(Choice E)** Hypertrophy of pyloric smooth muscles is seen in congenital pyloric stenosis, which causes projective vomiting and is typically diagnosed in infancy. The smooth muscle cells typically remain normal in diabetic gastroparesis.

**Educational objective:**

1



Feedback



Suspend



End Block





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### Educational objective:

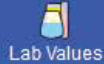
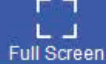
Diabetic gastroparesis results from the destruction of enteric neurons due to chronic hyperglycemia, leading to impaired relaxation and disordered and ineffective peristalsis. This causes delayed gastric emptying, which presents as postprandial fullness, regurgitation of undigested food, nausea, and vomiting.

### References

- [Diabetic gastroparesis.](#)







A 54-year-old man comes to the office due to increasing pain in the right upper quadrant, nausea, and unintentional weight loss. Vitals signs are within normal limits. BMI is 21 kg/m<sup>2</sup>. The patient appears cachectic and there is scleral icterus. The liver is palpable 3 cm below the right costal margin. No ascites is present. Laboratory studies reveal elevated bilirubin and alkaline phosphatase. Contrast CT scan of the abdomen demonstrates moderately dilated right and left intrahepatic bile ducts, with a vague area of delayed enhancement at their convergence. Biopsy of the lesion reveals columnar cells with hyperchromatic oval nuclei with prominent nucleoli arranged in glandular structures; mucin production with surrounding desmoplastic reaction is present. Which of the following is the most likely diagnosis?

- ☐ A. Cholangiocarcinoma
- ☐ B. Focal nodular hyperplasia
- ☐ C. Hepatic adenoma
- ☐ D. Hepatocellular carcinoma
- ☐ E. Metastatic colon cancer





unintentional weight loss. Vitals signs are within normal limits. BMI is 21 kg/m<sup>2</sup>. The patient appears cachectic and there is scleral icterus. The liver is palpable 3 cm below the right costal margin. No ascites is present. Laboratory studies reveal elevated **bilirubin** and alkaline phosphatase. Contrast CT scan of the abdomen demonstrates moderately **dilated** right and left intrahepatic bile ducts, with a vague area of delayed enhancement at their convergence. Biopsy of the lesion reveals **columnar cells** with hyperchromatic oval nuclei with prominent nucleoli arranged in glandular structures; mucin production with surrounding desmoplastic reaction is present. Which of the following is the most likely diagnosis?

- ☒ A. Cholangiocarcinoma (59%)
- ☐ B. Focal nodular hyperplasia (2%)
- ☐ C. Hepatic adenoma (7%)
- ☐ D. Hepatocellular carcinoma (8%)
- ☐ E. Metastatic colon cancer (21%)

Correct



59%



02 mins, 10 secs

Time Spent



09/08/2020

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2



Feedback



Suspend



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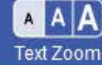
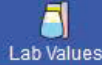
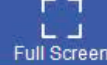
## Cholangiocarcinoma

<b>Epidemiology</b>	<ul style="list-style-type: none"><li>• Associated with primary sclerosing cholangitis</li></ul>
<b>Clinical presentation</b>	<ul style="list-style-type: none"><li>• Often clinically silent until advanced</li><li>• Nausea, weight loss, RUQ pain</li><li>• Jaundice, hepatomegaly, ± palpable gallbladder (Courvoisier sign)</li></ul>
<b>Laboratory abnormalities</b>	<ul style="list-style-type: none"><li>• Cholestatic pattern of liver injury (↑↑ alkaline phosphatase, hyperbilirubinemia)</li></ul>
<b>Imaging</b>	<ul style="list-style-type: none"><li>• Bile duct dilation in the absence of obstructing gallstone</li></ul>
<b>Histology</b>	<ul style="list-style-type: none"><li>• Adenocarcinoma with cuboidal or columnar cells with prominent nucleoli arranged in glandular structures</li><li>• + Mucin production, + desmoplastic response</li></ul>

**RUQ** = right upper quadrant.

This patient with weight loss, pain in the right upper quadrant (RUQ), and jaundice has radiographic and histologic findings consistent with **cholangiocarcinoma**, a malignancy of the bile duct epithelium. It is





RUQ = right upper quadrant.

This patient with weight loss, pain in the right upper quadrant (RUQ), and jaundice has radiographic and histologic findings consistent with **cholangiocarcinoma**, a malignancy of the bile duct epithelium. It is associated with primary sclerosing cholangitis; however, it may occur sporadically.

Cholangiocarcinoma is often clinically silent until late in the disease course, when the tumor obstructs bile drainage, leading to a characteristic **cholestatic pattern** of liver injury (elevated alkaline phosphatase, hyperbilirubinemia). Progressive weight loss, **RUQ pain**, **jaundice**, and **hepatomegaly** are typical, and occasionally, the gallbladder is palpable (Courvoisier sign).

Intraductal malignancies are often difficult to visualize radiographically but usually demonstrates **dilated bile ducts** in the absence of an obstructing gallstone. The most frequently involved site is at the **confluence of the right and left hepatic bile ducts** (Klatskin tumors), which may be visible as nonunion of the bile ducts (as in this patient). Most **cholangiocarcinomas** are **adenocarcinomas** characterized histologically by columnar epithelial cells with prominent nucleoli arranged in **glandular structures** with **mucin** production and significant desmoplasia (reactive fibrous tissue surrounding a malignant mass).

**(Choice B)** **Focal nodular hyperplasia** is a *benign*, nonencapsulated liver tumor that typically occurs in women. It is characterized by fibrous septa encasing normal hepatocytes and a central stellate scar, which





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

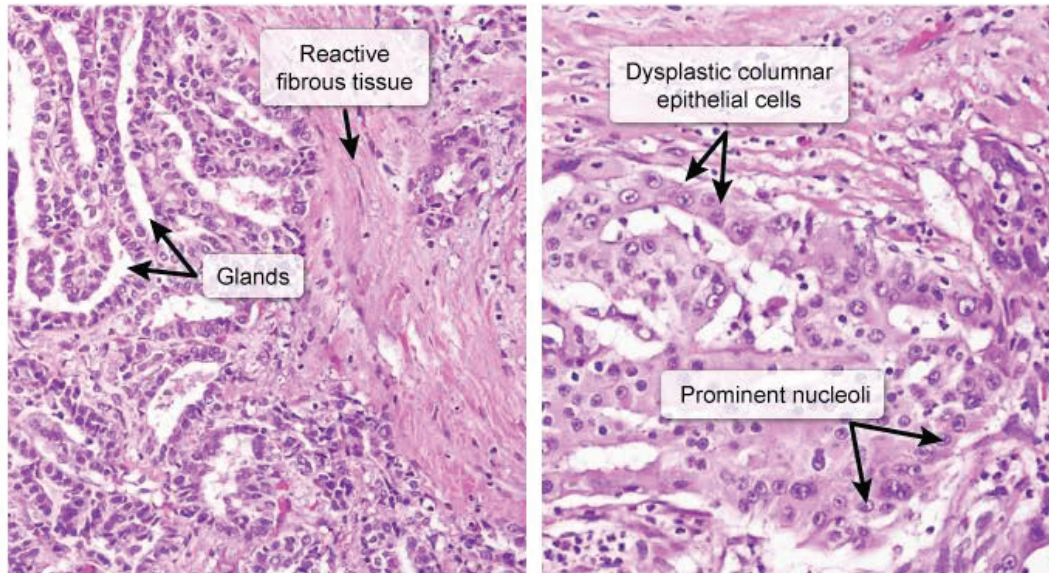
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## Cholangiocarcinoma



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Zoom Out

Reset

New | Existing

My Notebook

Usually causes multiple hepatic masses which are not seen on this patient's CT scan. In addition the

Block Time Remaining: 00:17:50

TUTOR

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2



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



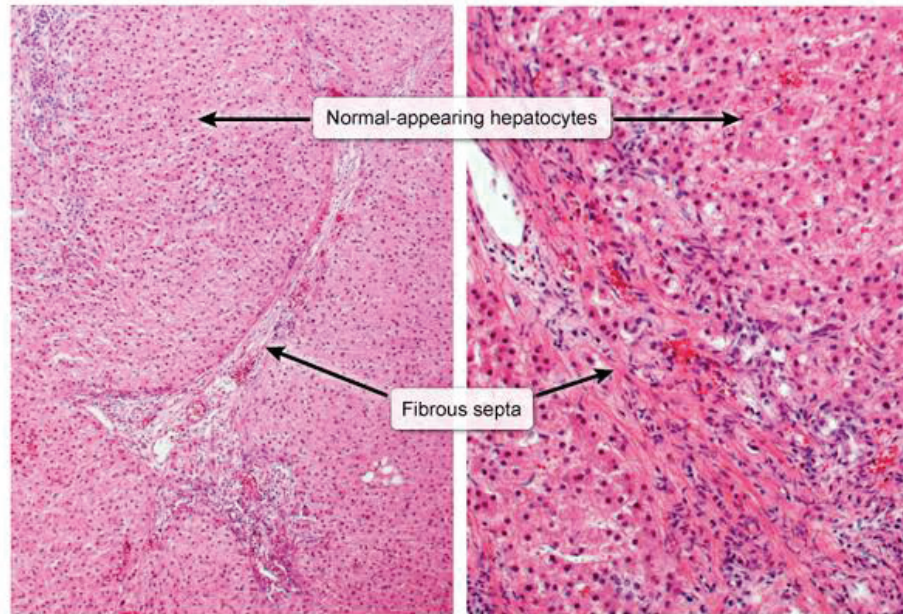
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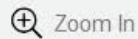
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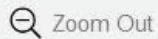
## Focal nodular hyperplasia



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Existing



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Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

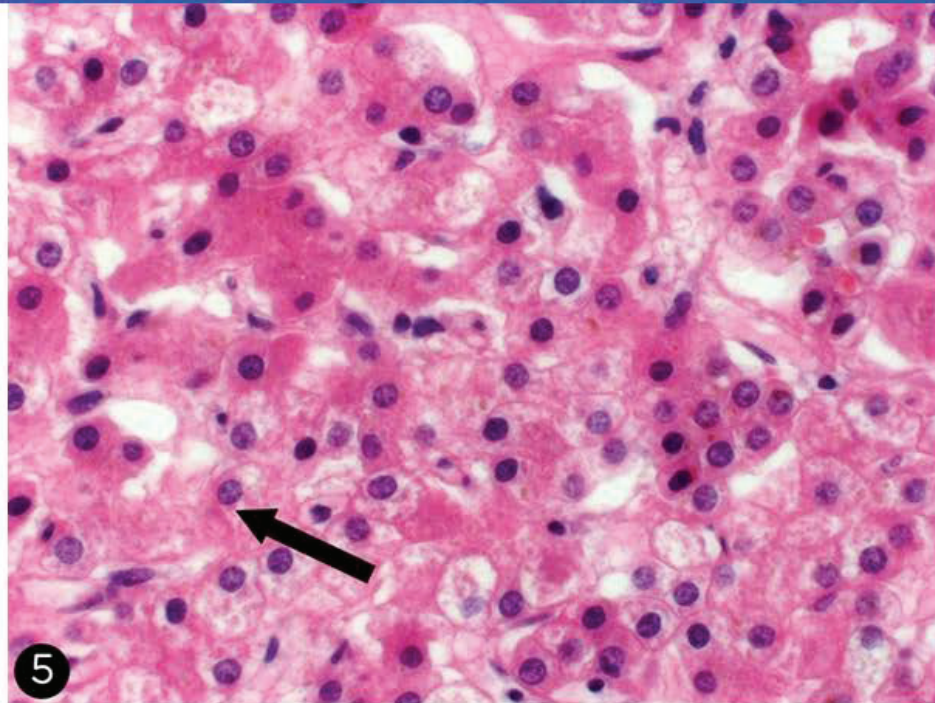


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Settings

## Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:17:50

TUTOR

<https://t.me/USMLEWorldStep1>

2



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



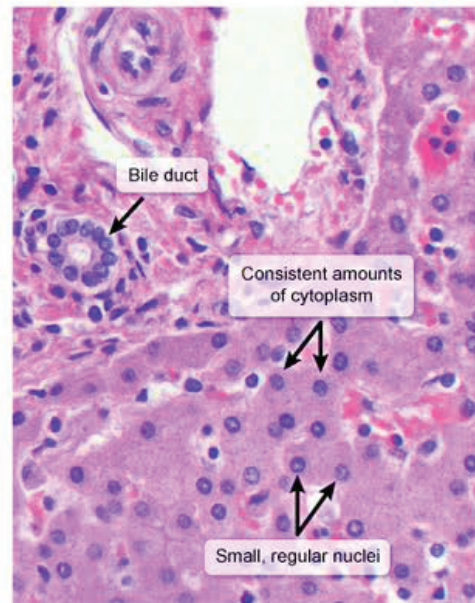
Text Zoom



Settings

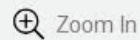
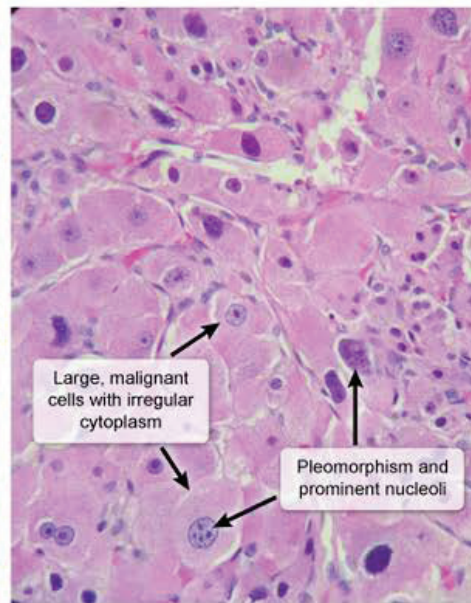
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Normal liver

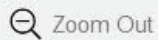


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Hepatocellular carcinoma



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Reset



New



Existing



My Notebook

My Notebook



2



Feedback



Suspend



End Block





**(Choice C)** **Hepatic adenomas** are *benign* lesions that develop most commonly in women taking oral contraceptives. Jaundice and weight loss are unexpected, and an abdominal CT scan usually demonstrates a solitary lesion in the hepatic parenchyma, not the biliary tree. Histology reveals relatively uniform hepatocytes arranged in thin cell plates without atypia.

**(Choice D)** **Hepatocellular carcinoma** is a malignant liver mass that most often develops in patients with cirrhosis. Microscopy demonstrates polygonal cells with abundant eosinophilic cytoplasm and prominent nucleoli.

**(Choice E)** **Metastatic colon cancer** is characterized by adenocarcinoma with gland formation; however, it usually causes multiple hepatic masses, which are not seen on this patient's CT scan. In addition, the location of the mass at the bifurcation of the common hepatic duct is characteristic of cholangiocarcinoma.

### Educational objective:

Cholangiocarcinoma is a malignancy of the bile duct epithelium that eventually obstructs biliary drainage, resulting in cholestasis (elevated alkaline phosphatase, hyperbilirubinemia) with jaundice, weight loss, pain in the right upper quadrant, and hepatomegaly. Imaging often demonstrates dilated bile ducts in the absence of an obstructive gallstone, and biopsy reveals an adenocarcinoma with columnar cells, mucin production, and a significant desmoplastic reaction.







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

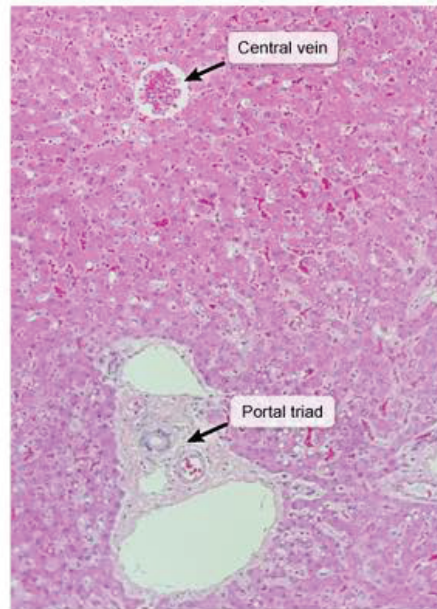
Text Zoom

Settings

(Choice C) Hepatic adenomas are benign lesions that develop most commonly in women taking oral

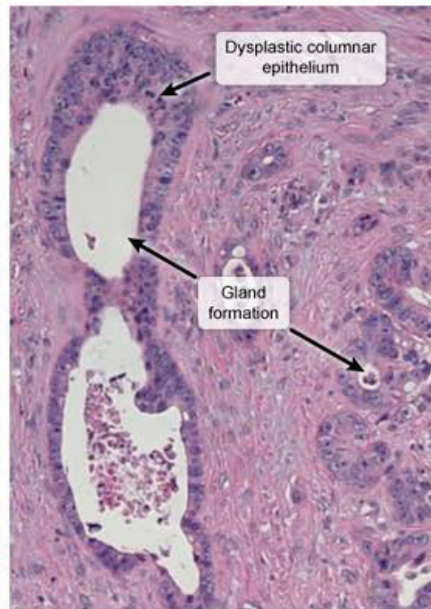
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Normal liver



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Metastatic colon cancer



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Zoom Out

Reset

New | Existing

My Notebook



2



Feedback



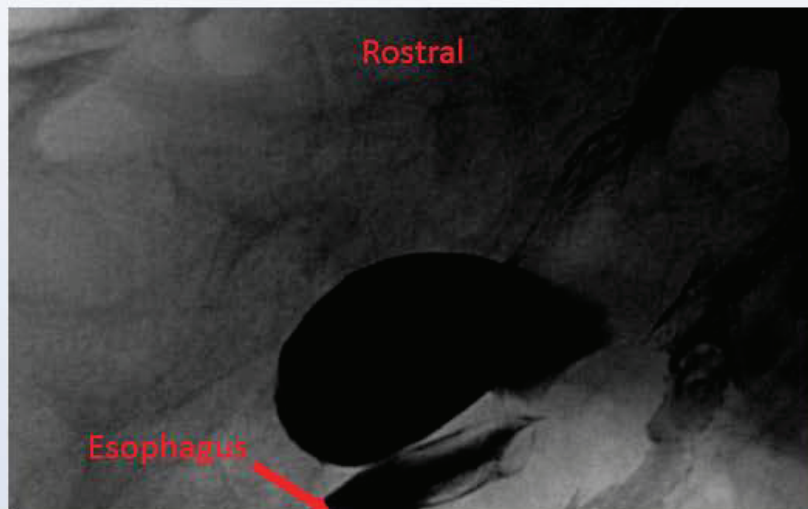
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A 74-year-old man comes to the office due to several months of choking spells, dysphagia, and cough. He has also had recurrent episodes of pneumonia. His other medical problems include hypertension and osteoarthritis. Blood pressure is 130/70 mm Hg. The patient has foul-smelling breath, but his oropharyngeal and neck examinations are normal. Cardiopulmonary examination is also normal. A barium swallow study is performed and reveals an abnormality in the upper esophagus, as shown in the image below.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



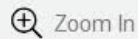
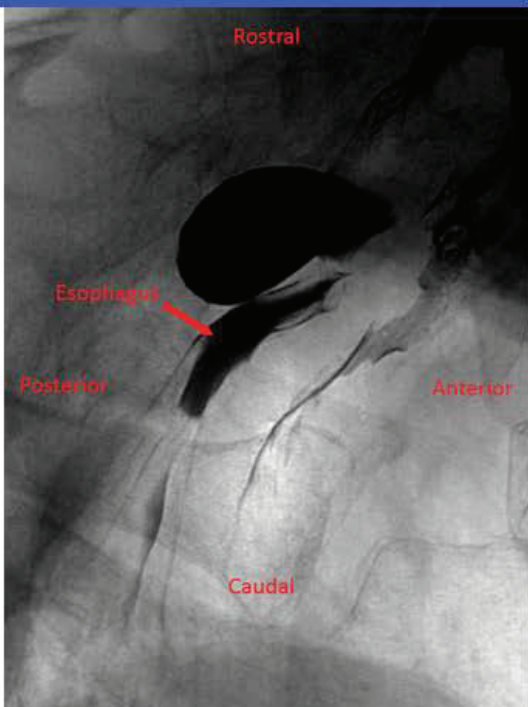
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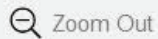
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below.

## Exhibit Display



Zoom In



Zoom Out



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New



Existing



My Notebook

My Notebook



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Which of the following mechanisms is the most likely cause of his symptoms?

- ☐ A. Cricopharyngeal motor dysfunction
- ☐ B. Degenerative changes of the myenteric plexus
- ☐ C. Increased intraluminal pressure in the stomach
- ☐ D. Retention cyst due to duct obstruction
- ☐ E. Scarring and traction of the esophagus

Submit

Block Time Remaining: 00:18:01

TUTOR

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Which of the following mechanisms is the most likely cause of his symptoms?

- ☒ A. Cricopharyngeal motor dysfunction (44%)
- ☐ B. Degenerative changes of the myenteric plexus (16%)
- ☐ C. Increased intraluminal pressure in the stomach (5%)
- ☐ D. Retention cyst due to duct obstruction (15%)
- ☐ E. Scarring and traction of the esophagus (17%)

Correct

44%

27 secs

11/29/2020

Block Time Remaining: 00:18:17

TUTOR

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

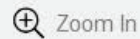
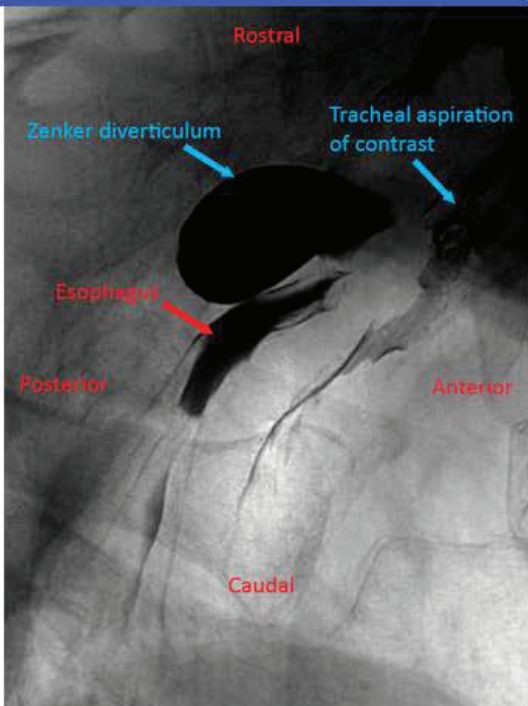


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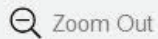


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## Exhibit Display



Zoom In



Zoom Out



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My Notebook

My Notebook



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Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



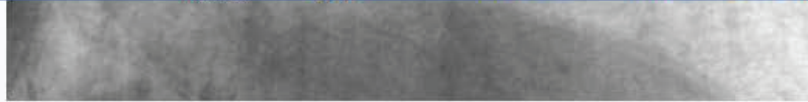
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Settings



Deglutition (swallowing) is a complex process that involves 3 phases:

1. In the voluntary oral phase, the food bolus is collected in the back of the mouth and lifted upward to the posterior wall of the pharynx.
2. This initiates the pharyngeal phase, which consists of involuntary pharyngeal muscle contractions that propel the food bolus to the esophagus.
3. During the esophageal phase, food stretches the walls of the esophagus, stimulating peristalsis just above the site of distension and moving the food downward. Relaxation of the lower esophageal sphincter (LES) follows, allowing the food bolus to enter the stomach.

Abnormal spasm or diminished relaxation of the cricopharyngeal muscles during swallowing (**cricopharyngeal motor dysfunction**) is thought to be the underlying mechanism of **Zenker diverticulum** formation. This process results in early **oropharyngeal dysphagia** with a feeling of food obstruction at the level of the neck and coughing/choking. Increased oropharyngeal intraluminal pressure eventually results in herniation of the pharyngeal mucosa through a zone of muscle weakness (**false diverticulum**) in the posterior hypopharynx (Killian triangle). Patients consequently develop food retention with



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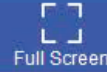
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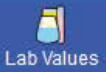
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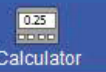
Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom

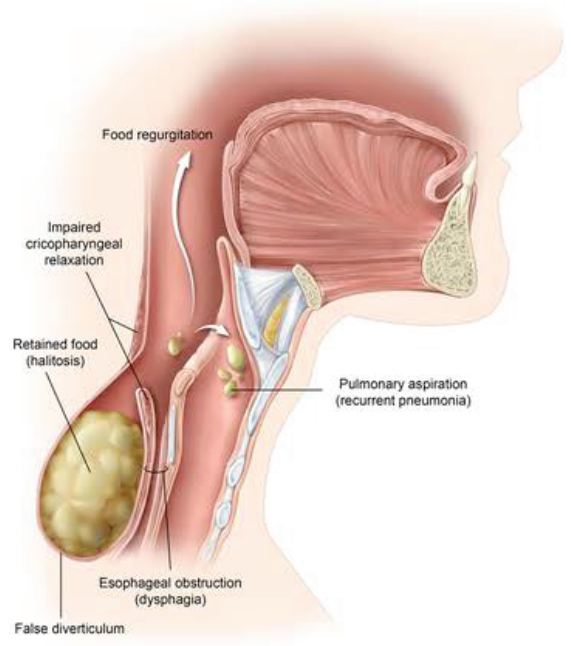


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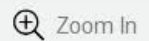
pharynx (UES) follows, allowing the food bolus to enter the stomach.

### Exhibit Display

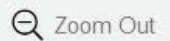
#### Zenker diverticulum



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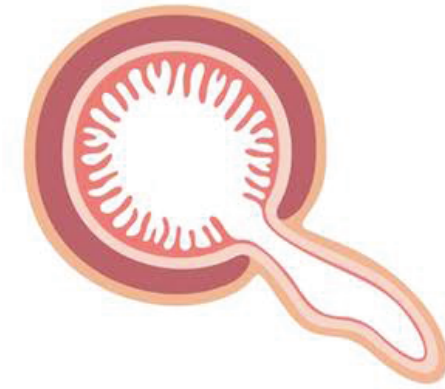
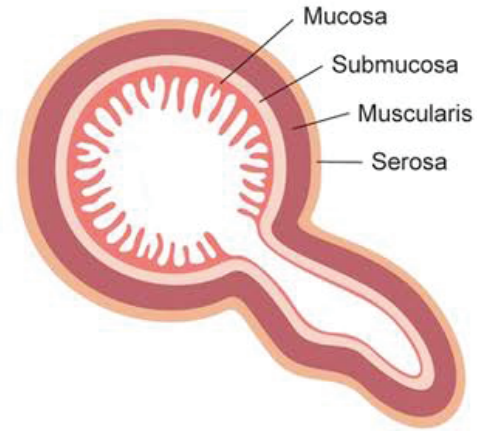
End Block

Exhibit Display

True & false diverticula

True diverticulum

Pseudodiverticulum



Examples:  
Meckel diverticula,  
normal appendix

Examples:  
Zenker esophageal diverticula,  
diverticulosis

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Previous



Next



Full Screen



Tutorial



Lab Values



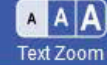
Notes



Calculator



Reverse Color



Text Zoom



Settings

posterior hypopharynx (Killian triangle). Patients consequently develop food retention with **halitosis/regurgitation**. **Pulmonary aspiration** of diverticular contents may also lead to recurrent pneumonia. As the diverticulum enlarges, it may become palpable as a lateral neck mass, and dysphagia can worsen due to luminal narrowing caused by extrinsic esophageal compression.

**(Choice B)** Degenerative changes of the myenteric plexus with impaired LES relaxation result in achalasia. Barium swallow typically shows esophageal dilation with esophagogastric junction narrowing ("bird's beak").

**(Choice C)** Mucosal tears around the gastroesophageal junction can be caused by increased intraluminal pressure in the stomach during prolonged or recurrent retching/vomiting (Mallory-Weiss syndrome).

**(Choice D)** Retention cysts form due to accumulation of trapped secretions following obstruction of a gland's duct. Chronic rhinosinusitis frequently causes mucus retention cysts in the maxillary sinus.

**(Choice E)** Mediastinal lymphadenitis (eg, due to tuberculosis, fungal infections) can cause scarring/traction of the mid-portion of the esophagus, resulting in the formation of true diverticula (containing all gut wall layers).

### Educational objective:

Diminished relaxation of cricopharyngeal muscles during swallowing results in increased intraluminal



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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



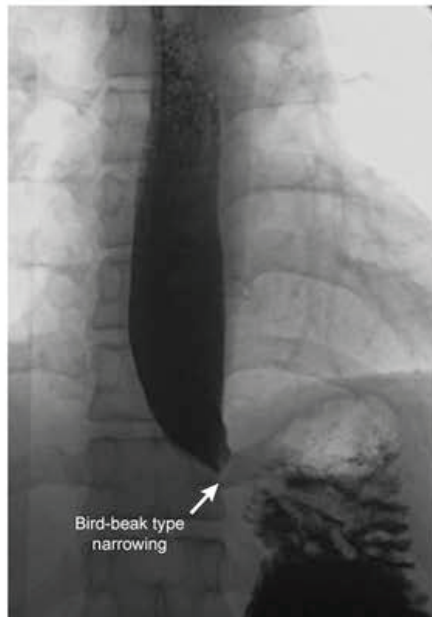
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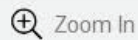
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## Exhibit Display

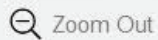
## Achalasia

Bird-beak type  
narrowing

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Existing



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1



Feedback



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

("bird's beak").

**(Choice C)** Mucosal tears around the gastroesophageal junction can be caused by increased intraluminal pressure in the stomach during prolonged or recurrent retching/vomiting (Mallory-Weiss syndrome).

**(Choice D)** Retention cysts form due to accumulation of trapped secretions following obstruction of a gland's duct. Chronic rhinosinusitis frequently causes mucus retention cysts in the maxillary sinus.

**(Choice E)** Mediastinal lymphadenitis (eg, due to tuberculosis, fungal infections) can cause scarring/traction of the mid-portion of the esophagus, resulting in the formation of true diverticula (containing all gut wall layers).

### Educational objective:

Diminished relaxation of cricopharyngeal muscles during swallowing results in increased intraluminal pressure in the oropharynx. This may eventually cause the mucosa to herniate through a zone of muscle weakness in the posterior hypopharynx, forming a Zenker (false) diverticulum, which presents in elderly patients with oropharyngeal dysphagia, halitosis, regurgitation, and recurrent aspiration.

### References

- [Zenker's diverticulum: exploring treatment options.](#)



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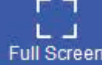




Previous



Next



Full Screen



Tutorial



Lab Values



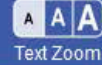
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 52-year-old man comes to the office for a painless mass in his right groin. He noticed the mass several weeks ago, and it has slowly enlarged. The patient has a history of HIV, for which he takes antiretroviral therapy. He has not had any new sexual partners recently. Temperature is 37.1 C (98.8 F). On examination, several enlarged, hard lymph nodes are palpated in the right inguinal area inferior to the inguinal ligament. An excisional biopsy is performed, and histopathology shows malignant cells. The malignant cells found in this patient most likely originated from which of the following sites?

- ☐ A. Dome of the bladder
- ☐ B. Lateral lobe of the prostate
- ☐ C. Orifice of the anal canal
- ☐ D. Upper pole of the testes
- ☐ E. Upper third of the rectum

**Submit**

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 52-year-old man comes to the office for a painless mass in his right groin. He noticed the mass several weeks ago, and it has slowly enlarged. The patient has a history of HIV, for which he takes antiretroviral therapy. He has not had any new sexual partners recently. Temperature is 37.1 C (98.8 F). On examination, several enlarged, hard lymph nodes are palpated in the right inguinal area inferior to the inguinal ligament. An excisional biopsy is performed, and histopathology shows malignant cells. The malignant cells found in this patient most likely originated from which of the following sites?

- ☐ A. Dome of the bladder (5%)
- ☐ B. Lateral lobe of the prostate (12%)
- ☒ C. Orifice of the anal canal (54%)
- ☐ D. Upper pole of the testes (17%)
- ☐ E. Upper third of the rectum (10%)

Correct

 54%  
Answered correctly 01 min, 04 secs  
Time Spent 12/21/2020  
Last Updated

Block Time Remaining: 00:19:21

TUTOR

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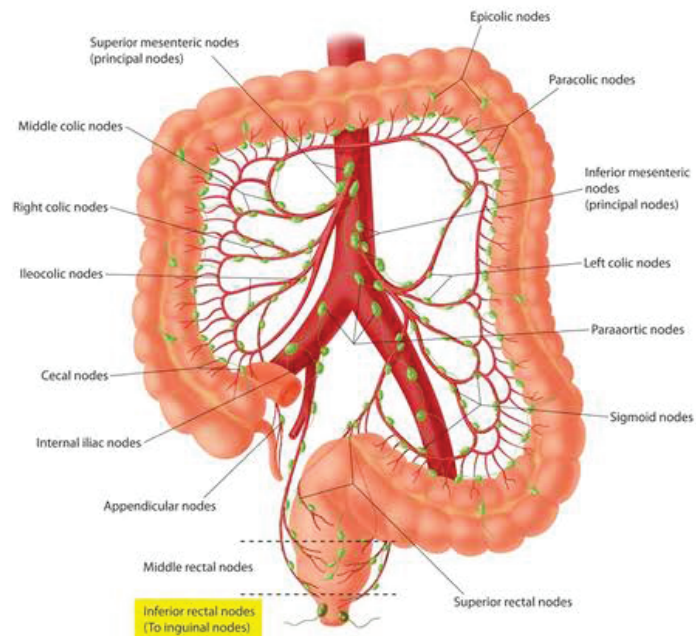
Suspend



End Block

### Exhibit Display

#### Lymph nodes & vessels of large intestine



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Previous



Next



Full Screen



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Notes



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Settings

This patient has palpable, firm **superficial inguinal lymph nodes**. These nodes overlie the femoral nerve, artery, and vein in the femoral triangle, a region bound by the inguinal ligament, sartorius muscle, and adductor longus muscle. The superficial inguinal nodes drain **most cutaneous lymph** from the **umbilicus down**, including the external genitalia and anus (below the dentate line). In this patient, metastasis from a malignancy around the orifice of the **anal canal** most likely explains his inguinal lymphadenopathy.

**Exceptions** to this drainage pattern include the **glans penis** and skin of the **posterior calf** (popliteal lymph nodes), which bypass the superficial inguinal nodes to drain into the deep inguinal lymph nodes.

**(Choice A)** Lymph from the superior portion of the bladder drains to the external iliac nodes whereas lymph from the inferior portion of the bladder drains to the internal iliac nodes.

**(Choice B)** Lymph from the prostate drains primarily to the internal iliac nodes.

**(Choice D)** Lymph from the testes parallels the blood supply from the testicular arteries, which arise directly from the abdominal aorta. As such, testicular lymph drains to the abdominal para-aortic (retroperitoneal) lymph nodes.

**(Choice E)** Lymph from the upper third of the rectum drains to the inferior mesenteric lymph nodes.

**Educational objective:**



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

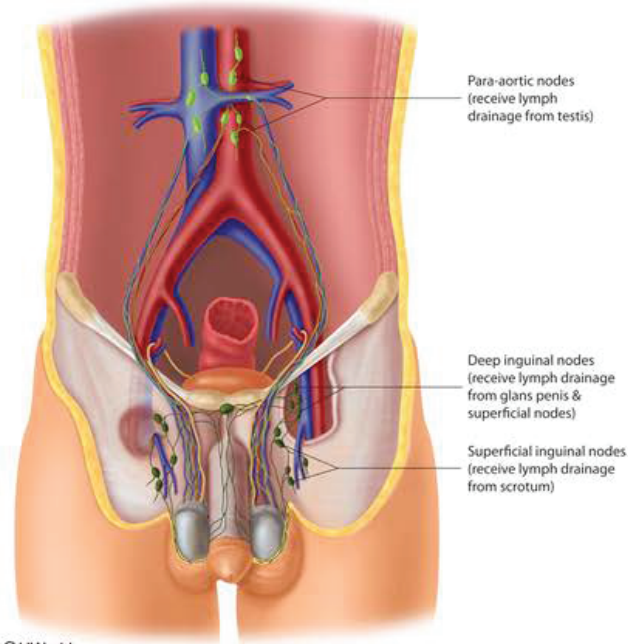
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## Exhibit Display

## Lymph vessels &amp; nodes of male genitalia



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Text Zoom



Settings

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**(Choice B)** Lymph from the prostate drains primarily to the internal iliac nodes.

**(Choice D)** Lymph from the testes parallels the blood supply from the testicular arteries, which arise directly from the abdominal aorta. As such, testicular lymph drains to the abdominal para-aortic (retroperitoneal) lymph nodes.

**(Choice E)** Lymph from the upper third of the rectum drains to the inferior mesenteric lymph nodes.

### Educational objective:

Most of the cutaneous lymph from the umbilicus down, including the anus below the dentate line, drains to the superficial inguinal lymph nodes. Exceptions are the glans penis and posterior calf, which drain to the deep inguinal nodes.

Anatomy  
Subject

Gastrointestinal & Nutrition  
System

Lymphatic drainage  
Topic

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Suspend



End Block





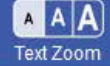
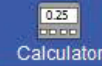
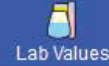
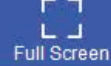
A 55-year-old Caucasian male is found on colonoscopy to have a solitary mass in his sigmoid colon.

Biopsy is consistent with colon cancer, and surgery is scheduled. Which of the following features would carry the worst prognosis in this patient?

- ☐ A. Presence of clinical symptoms
- ☐ B. Tumor penetration into the muscularis propria
- ☐ C. Poor differentiation of tumor cells
- ☐ D. High degree of tumor cell aneuploidy
- ☐ E. High number of mitotic figures

Submit





A 55-year-old Caucasian male is found on colonoscopy to have a solitary mass in his sigmoid colon.

Biopsy is consistent with colon cancer, and surgery is scheduled. Which of the following features would carry the worst prognosis in this patient?

- ☐ A. Presence of clinical symptoms (2%)
- ☒ B. Tumor penetration into the muscularis propria (76%)
- ☐ C. Poor differentiation of tumor cells (13%)
- ☐ D. High degree of tumor cell aneuploidy (2%)
- ☐ E. High number of mitotic figures (5%)

Correct

76%  
Answered correctly

15 secs  
Time Spent

01/30/2021  
Last Updated

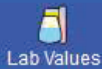
Explanation

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The extent of tumor expansion is characterized by the **stage** of a tumor. The degree of tumor differentiation (from well-differentiated to anaplastic) is referred to as the **grade**. Tumor stage is the most important criteria for determining prognosis.

If the tumor is confined to the mucosa (stage A), the patient has 90%+ chance of 5-year survival. If it involves the muscular layer, 5-year survival rate is 70-80%. Lymph node involvement (stage C) and distant metastasis (stage D) have poor prognosis.

**(Choice A)** Colon adenocarcinomas tend to be asymptomatic at early stages, which is why screening colonoscopies are so important. By the time symptoms appear, tumor size is substantial. Clinical manifestations, however, do not correlate as well with prognosis as the stage of an adenocarcinoma does.

**(Choices C, D and E)** Tumor cell differentiation, degree of aneuploidy, and number of mitotic figures determines the grade of the tumor. Remember that stage is more important than grade in determining the prognosis of colon cancer.

### Educational Objective:

Prognosis of colorectal adenocarcinoma is directly related to the stage of the tumor (not to the grade!).







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

important criteria for determining prognosis.

If the tumor is confined to the mucosa (stage A), the patient has 90%+ chance of 5-year survival. If it involves the muscular layer, 5-year survival rate is 70-80%. Lymph node involvement (stage C) and distant metastasis (stage D) have poor prognosis.

**(Choice A)** Colon adenocarcinomas tend to be asymptomatic at early stages, which is why screening colonoscopies are so important. By the time symptoms appear, tumor size is substantial. Clinical manifestations, however, do not correlate as well with prognosis as the stage of an adenocarcinoma does.

**(Choices C, D and E)** Tumor cell differentiation, degree of aneuploidy, and number of mitotic figures determines the grade of the tumor. Remember that stage is more important than grade in determining the prognosis of colon cancer.

### Educational Objective:

Prognosis of colorectal adenocarcinoma is directly related to the stage of the tumor (not to the grade!).

Pathology

Gastrointestinal &amp; Nutrition

Colorectal polyps and cancer

Subject

System

Topic

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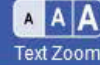
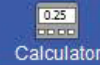
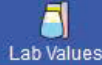
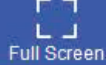
Feedback



Suspend



End Block



A 40-year-old woman comes to the office with a 4-week history of diarrhea accompanied by occasional abdominal bloating. She has noticed that her stools contain mucus but has not seen any blood. The patient also has intermittent mild heartburn. She has no fevers, chills, or weight loss. The patient has also noticed an unpleasant taste with dairy products and now avoids them. Past medical history is significant for chronic allergic rhinitis. Current medications include only a multivitamin supplement. Vital signs and physical examination are normal. After a basic evaluation, the patient is started on a trial of diphenoxylate therapy. Which of the following is the primary target of this drug?

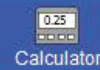
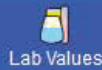
- ☐ A. Absorption
- ☐ B. Digestion
- ☐ C. Inflammation
- ☐ D. Motility
- ☐ E. Secretion

**Submit**

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TUTOR

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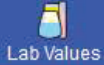
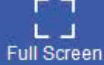


A 40-year-old woman comes to the office with a 4-week history of diarrhea accompanied by occasional abdominal bloating. She has noticed that her stools contain mucus but has not seen any blood. The patient also has intermittent mild heartburn. She has no fevers, chills, or weight loss. The patient has also noticed an unpleasant taste with dairy products and now avoids them. Past medical history is significant for chronic allergic rhinitis. Current medications include only a multivitamin supplement. Vital signs and physical examination are normal. After a basic evaluation, the patient is started on a trial of diphenoxylate therapy. Which of the following is the primary target of this drug?

- ☐ A. Absorption (16%)
- ☐ B. Digestion (13%)
- ☐ C. Inflammation (10%)
- ☒ D. Motility (42%)
- ☐ E. Secretion (15%)







This patient has uncomplicated **diarrhea** with benign findings on initial examination and evaluation. Common causes include irritable bowel syndrome and functional diarrhea. In such cases, empiric symptomatic therapy is often considered prior to more complex testing.

**Diphenoxylate** is an opioid anti-diarrheal agent structurally related to meperidine. It binds to **mu opiate receptors** in the gastrointestinal tract and **slows motility**. Low doses relieve diarrhea without other significant opiate effects. However, higher doses can produce morphine-like euphoria and physical dependence. To discourage abuse, diphenoxylate is combined with atropine, which produces adverse symptoms (dry mouth, blurry vision, nausea) if taken in high doses. Loperamide is another low-potency opioid agonist used in the symptomatic treatment of diarrhea. Common side effects of these drugs include rebound constipation and mild sedation. They should not be used in diarrhea due to toxin-producing or invasive organisms (eg, *Shigella*, *Salmonella*) or *Clostridium difficile* infections.

**(Choices A and B)** Substances that are poorly digested or absorbed can retain fluid in the intestinal lumen and cause diarrhea. Lactase enzyme supplements are used in patients with lactase deficiency who have diarrhea due to undigested dietary lactose. Patients with exocrine pancreatic deficiency often have diarrhea due to undigested fats; pancreatic enzyme supplements are useful in these individuals.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choices A and B)** Substances that are poorly digested or absorbed can retain fluid in the intestinal lumen and cause diarrhea. Lactase enzyme supplements are used in patients with lactase deficiency who have diarrhea due to undigested dietary lactose. Patients with exocrine pancreatic deficiency often have diarrhea due to undigested fats; pancreatic enzyme supplements are useful in these individuals.

**(Choice C)** Ulcerative colitis and Crohn disease are inflammatory bowel diseases that commonly present with diarrhea. Inflammation of the gut causes mucous, proteinaceous, and bloody discharge that leads to diarrhea. Treatment involves anti-inflammatory drugs, corticosteroids, and other immunosuppressive agents. This patient lacks inflammatory features.

**(Choice E)** Secretory diarrhea can be due to many different substances (eg, vasoactive intestinal peptide, bacterial toxins) that increase secretions. Agents that target secretory diarrhea include bismuth subsalicylate, octreotide, and possibly some probiotic preparations.

**Educational objective:**

Diphenoxylate is an opioid antidiarrheal drug that binds mu opiate receptors in the gut to slow motility. Overuse can lead to euphoria and physical dependence. To discourage abuse, diphenoxylate is combined with atropine, which induces adverse effects if taken in high doses.



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

Experimental gastric function monitoring in healthy subjects before, during and after a meal shows an initial rise, peak, and then decline in gastric acid production. Which of the following helps most to down-regulate gastric secretion after a meal?

- ☐ A. Basal secretion
- ☐ B. Cephalic phase
- ☐ C. Gastrin release
- ☒ D. Intestinal influences
- ☐ E. Receptive relaxation
- ☐ F. Postprandial alkaline tide

**Submit**

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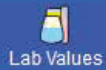


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Experimental gastric function monitoring in healthy subjects before, during and after a meal shows an initial rise, peak, and then decline in gastric acid production. Which of the following helps most to down-regulate gastric secretion after a meal?

- ☐ A. Basal secretion (3%)
- ☐ B. Cephalic phase (4%)
- ☐ C. Gastrin release (10%)
- ☒ D. Intestinal influences (60%)
- ☐ E. Receptive relaxation (5%)
- ☐ F. Postprandial alkaline tide (15%)

Correct

 60%  
Answered correctly

 15 secs  
Time Spent

 10/20/2020  
Last Updated





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Classically, the stimulation of acid secretion within the stomach is separated into three phases: cephalic, gastric, and intestinal. The cephalic phase is mediated primarily by cholinergic and vagal mechanisms, and is triggered by the thought, sight, smell, and taste of food. The gastric phase is mediated by the presence of gastrin (which stimulates histamine secretion and therefore, indirectly, acid secretion), and is triggered by the chemical stimulus of food and distension of the stomach. The intestinal phase is initiated when protein-containing food enters the duodenum, but this phase plays only a minor role in stimulating gastric acid secretion.

In fact, intestinal influences are effective in down-regulating gastric acid secretion after a meal. The ileum and colon release peptide YY, which binds to receptors on the endocrine, histamine-containing cells described as enterochromaffin-like (ECLs). Such binding counteracts the cephalic and gastric phases of acid secretion by inhibiting gastrin-stimulated histamine release from ECLs. Other factors that inhibit acid secretion include somatostatin and prostaglandins.

**(Choice A)** Basal gastric secretion has been defined as the gastric juices secreted in the absence of intentional or avoidable stimuli (essentially, the "baseline" gastric acid secretion). Basal gastric secretion is not an important factor in the down-regulation of postprandial gastric secretion.

**(Choices B and C)** The cephalic and gastric phases both stimulate gastric acid secretion, not down-



1



Feedback



Suspend



End Block



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice A)** Basal gastric secretion has been defined as the gastric juices secreted in the absence of intentional or avoidable stimuli (essentially, the "baseline" gastric acid secretion). Basal gastric secretion is not an important factor in the down-regulation of postprandial gastric secretion.

**(Choices B and C)** The cephalic and gastric phases both stimulate gastric acid secretion, not down-regulate it.

**(Choice E)** Receptive relaxation is a reflex that allows the gastric fundus to dilate in anticipation of food passing through the pharynx and esophagus. It is not an important factor in the down-regulation of postprandial gastric secretion.

**(Choice F)** Postprandial alkaline tide is defined as an increase in plasma  $\text{HCO}_3^-$  and decrease in plasma  $\text{Cl}^-$  secondary to the surge of acid within the gastric lumen. It is not an important factor in the down-regulation of postprandial gastric secretion.

**Educational Objective:**

The cephalic and gastric phases stimulate gastric acid secretion, while intestinal influences tend to reduce gastric acid secretion.



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Feedback

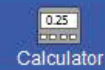
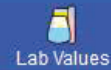


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A 32-year-old woman comes to the office for bloating, intermittent diarrhea, and abdominal cramps. Her symptoms have been ongoing for many years and are usually triggered by meals. Medical history and family history are both unremarkable. Vital signs are within normal limits. BMI is 27 kg/m<sup>2</sup>. The patient is well-appearing, and the abdomen is soft and nontender. Laboratory analysis is unremarkable. The patient is diagnosed with irritable bowel syndrome, and it is recommended that she take loperamide and consume an adequate amount of dietary fiber. After reading about her disorder on the internet, the patient decides to manage her symptoms with a strict vegan diet. Which of the following should be provided as a nutritional supplement for this patient?

- ☐ A. Calcium
- ☐ B. Folic acid
- ☐ C. Magnesium
- ☐ D. Niacin
- ☐ E. Thiamine





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

symptoms have been ongoing for many years and are usually triggered by meals. Medical history and family history are both unremarkable. Vital signs are within normal limits. BMI is 27 kg/m<sup>2</sup>. The patient is well-appearing, and the abdomen is soft and nontender. Laboratory analysis is unremarkable. The patient is diagnosed with irritable bowel syndrome, and it is recommended that she take loperamide and consume an adequate amount of dietary fiber. After reading about her disorder on the internet, the patient decides to manage her symptoms with a strict vegan diet. Which of the following should be provided as a nutritional supplement for this patient?

- ✓ ☒ A. Calcium (35%)
- ☐ B. Folic acid (31%)
- ☐ C. Magnesium (5%)
- ☐ D. Niacin (13%)
- ☐ E. Thiamine (14%)

Correct

35%



18 secs



01/17/2021

Block Time Remaining: 00:21:24

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1



Feedback



Suspend



End Block



## Explanation

Vegan diet	
Composition	<ul style="list-style-type: none"><li>• Complete abstinence from animal-derived foods</li><li>• Emphasis on fruits, vegetables, legumes</li></ul>
Potential benefits	<ul style="list-style-type: none"><li>• Lower blood glucose &amp; cholesterol</li><li>• Reduced risk of cardiovascular disease (eg, heart disease, stroke)</li></ul>
Potential nutritional deficiencies	<ul style="list-style-type: none"><li>• Common: vitamin B<sub>12</sub>, vitamin D, calcium</li><li>• Possible: iodine, iron, zinc</li></ul>

Individuals who adhere to a **vegan diet** consume only plant-based foods and avoid all meat and other animal-derived products (eg, milk). Adherence to a vegan diet is associated with a decreased risk of type 2 diabetes, hypercholesterolemia, coronary artery disease, and stroke.

However, most people obtain a significant portion of daily calcium and vitamin D requirements from dairy







diabetes, hypercholesterolemia, coronary artery disease, and stroke.

However, most people obtain a significant portion of daily calcium and vitamin D requirements from dairy products; individuals on a vegan diet often consume **less calcium and vitamin D** than non-vegans.

Supplementation is recommended to avoid long-term consequences, including **osteoporosis** and bone fractures. **Cobalamin (vitamin B<sub>12</sub>) deficiency** can also be seen in vegans, leading to megaloblastic anemia and subacute combined degeneration of the dorsal columns of the spinal cord.

**(Choice B)** Folic acid is found in many plant-based products, including leafy vegetables and legumes.

Supplementation is recommended during pregnancy to prevent fetal neural tube defects but is not needed in a vegan diet.

**(Choice C)** Magnesium is found in almost all foods. Hypomagnesemia can cause neuromuscular excitability (eg, tetany) and arrhythmias but is usually related to fluid losses (eg, diarrhea, diuretic use) or heavy alcohol use rather than dietary inadequacy.

**(Choice D)** Niacin deficiency can lead to pellagra, characterized by diarrhea, dermatitis, and possible dementia. Deficiency usually occurs in severely malnourished individuals (eg, alcohol use disorder, anorexia nervosa); however, niacin is found in a number of common vegetables and deficiency is uncommon in a vegan diet.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice C)** Magnesium is found in almost all foods. Hypomagnesemia can cause neuromuscular excitability (eg, tetany) and arrhythmias but is usually related to fluid losses (eg, diarrhea, diuretic use) or heavy alcohol use rather than dietary inadequacy.

**(Choice D)** Niacin deficiency can lead to pellagra, characterized by diarrhea, dermatitis, and possible dementia. Deficiency usually occurs in severely malnourished individuals (eg, alcohol use disorder, anorexia nervosa); however, niacin is found in a number of common vegetables and deficiency is uncommon in a vegan diet.

**(Choice E)** Thiamine is found in legumes, brown rice, and whole-grain cereal. Thiamine deficiency is most common in those with chronic alcoholism and leads to Wernicke-Korsakoff syndrome (oculomotor dysfunction, ataxia, memory loss).

### Educational objective:

Individuals on a vegan diet are at increased risk for deficiencies in calcium and vitamin D.

Supplementation is recommended to avoid long term consequences, including osteoporosis and bone fractures. Cobalamin (vitamin B<sub>12</sub>) deficiency can also occur.

### References

- [Bone nutrients for vegetarians.](#)



1



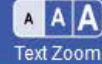
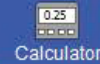
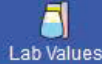
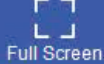
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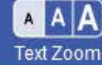
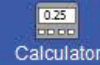
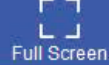


A 34-year-old woman is found dead in her apartment. Medical history is significant for substance abuse and a prior hospitalization for upper extremity cellulitis. An autopsy examination is performed. A ruptured plaque in the proximal anterior descending artery with an overlying occlusive thrombus is found. Incidentally, a 4-cm hepatic mass in the right lobe of the liver is also found. The mass is lighter than the surrounding liver tissue and appears lobulated with a central, gray-white, depressed stellate scar from which fibrous septae radiate to the periphery. The rest of the liver is normal. No additional abnormalities are noted on autopsy. Which of the following is the most likely diagnosis of this patient's liver lesion?

- ☐ A. Focal nodular hyperplasia
- ☐ B. Hepatic adenoma
- ☐ C. Hepatic hemangioma
- ☐ D. Hepatocellular carcinoma
- ☐ E. Hydatid cyst

**Submit**

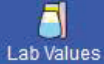
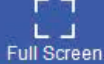




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- ☒ A. Focal nodular hyperplasia (26%)
- ☐ B. Hepatic adenoma (21%)
- ☐ C. Hepatic hemangioma (8%)
- ☐ D. Hepatocellular carcinoma (25%)
- ☐ E. Hydatid cyst (16%)





This patient's liver mass is characteristic of **focal nodular hyperplasia** (FNH), a nonmalignant lesion that most commonly occurs in **young women**. FNH is thought to result from a hepatic vascular abnormality causing localized hyperperfusion with a secondary hyperplastic response. Classically, the lesions appear as small, solitary, **pale nodules** composed of cords of normal-appearing hepatocytes and a **central stellate scar** with **fibrous septae** that surround abnormally large hepatic arterial branches.

FNH is **benign** and typically does not enlarge, undergo malignant transformation, or rupture; therefore, most cases do not require treatment. These lesions are usually **asymptomatic** and discovered incidentally during autopsy or abdominal imaging for a different condition. The diagnosis is confirmed most often by observing a characteristic solitary mass on imaging with features indicating the arterial origin of FNH (eg, enhancement with contrast in the arterial phase).

**(Choice B)** Hepatic adenoma is a benign liver lesion that is strongly associated with oral contraceptive use and may undergo malignant transformation or rupture. Although it can also be discovered incidentally, a hepatic adenoma will usually appear as an irregular, tan-colored group of nodules composed of large plates of **adenoma cells** with an absence of normal hepatic architecture (no portal structures or bile ducts).

**(Choice C)** Hepatic hemangioma is the most common benign hepatic tumor but would be characterized by







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Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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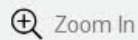
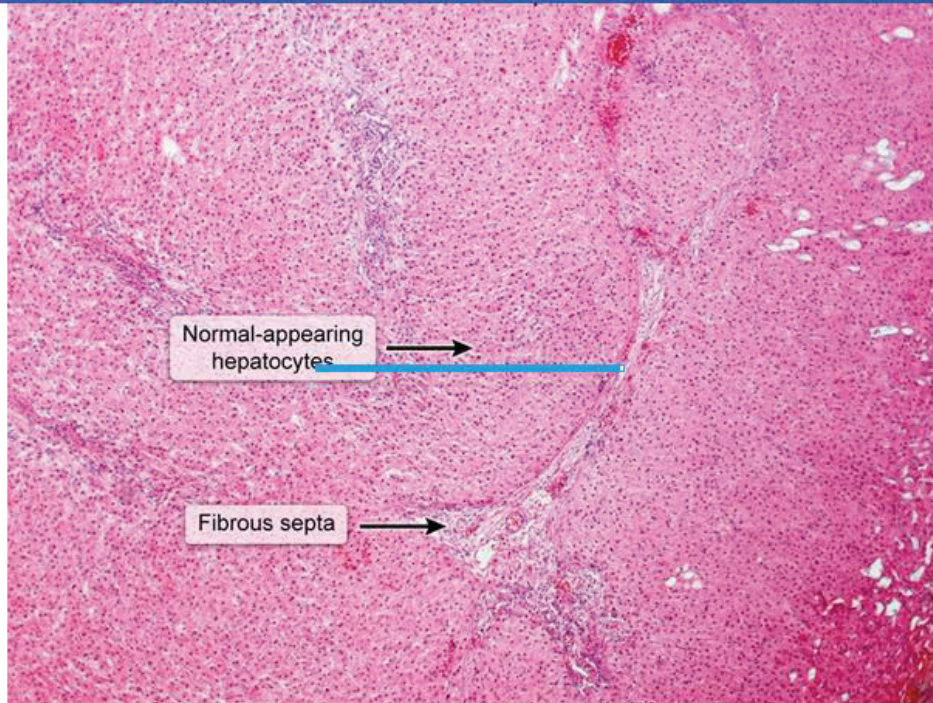


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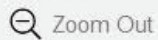


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## Exhibit Display



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enhancement with contrast in the arterial phase).

**(Choice B)** Hepatic adenoma is a benign liver lesion that is strongly associated with oral contraceptive use and may undergo malignant transformation or rupture. Although it can also be discovered incidentally, a hepatic adenoma will usually appear as an irregular, tan-colored group of nodules composed of large plates of **adenoma cells** with an absence of normal hepatic architecture (no portal structures or bile ducts).

**(Choice C)** Hepatic hemangioma is the most common benign hepatic tumor but would be characterized by a dark, vascular tumor with areas of hemorrhage. Histologically, these tumors display **cavernous vascular compartments** lined by epithelium and filled with red blood cells.

**(Choice D)** Hepatocellular carcinoma (HCC) is a malignant liver tumor that usually develops in the setting of underlying chronic liver disease (eg, chronic viral hepatitis, alcohol-induced cirrhosis). Well-differentiated HCC can appear similar to normal liver tissue; however, these tumors are typically larger, irregular, and symptomatic (eg, abdominal pain, elevated LFTs) with areas of hemorrhage on gross examination.

**(Choice E)** Hydatid cysts are caused by the larvae form of *Echinococcus granulosus*, a canine tapeworm. This pathogen is rare in the United States, and hepatic echinococcal lesions would present as fluid-filled cysts lined by a membrane derived from the parasite.

**Educational objective:**





Mark

Previous

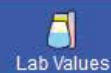
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Full Screen



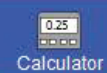
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Lab Values



Notes



Calculator



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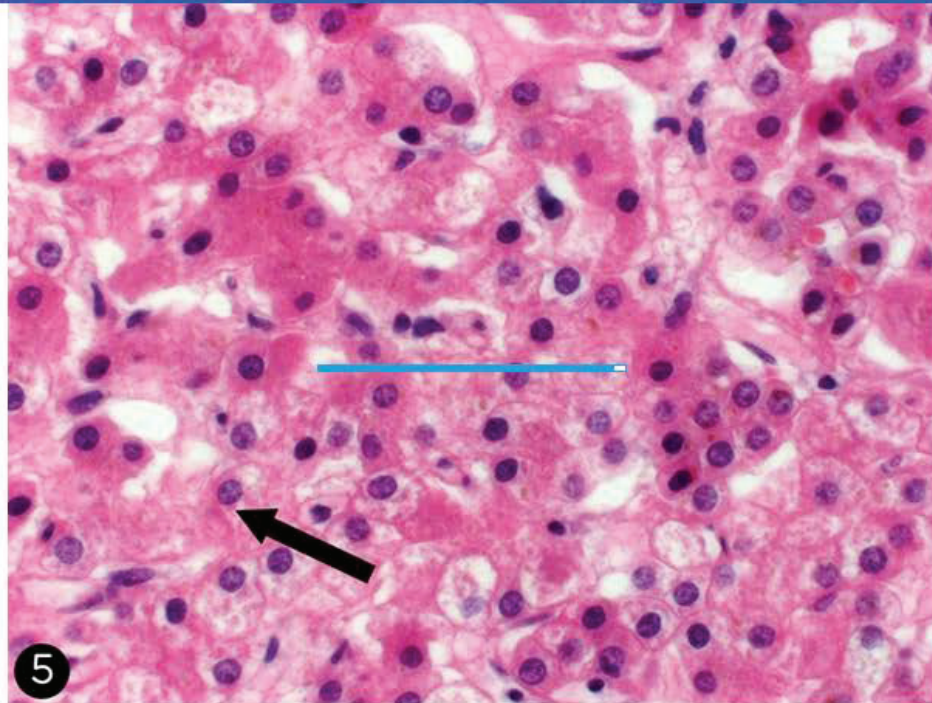
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enhancement with contrast in the arterial phase)

## Exhibit Display



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My Notebook

Educational objective:

Block Time Remaining: 00:22:16

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Feedback

Suspend



End Block



Mark

Previous

Next



Full Screen



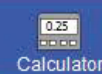
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Lab Values



Notes



Calculator



Reverse Color



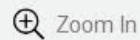
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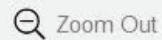
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enhancement with contrast in the arterial phase)

## Exhibit Display



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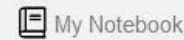
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My Notebook

Educational objective:

Block Time Remaining: 00:22:16

TUTOR

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

a dark, vascular tumor with areas of hemorrhage. Histologically, these tumors display **cavernous vascular compartments** lined by epithelium and filled with red blood cells.

**(Choice D)** Hepatocellular carcinoma (HCC) is a malignant liver tumor that usually develops in the setting of underlying chronic liver disease (eg, chronic viral hepatitis, alcohol-induced cirrhosis). Well-differentiated HCC can appear similar to normal liver tissue; however, these tumors are typically larger, irregular, and symptomatic (eg, abdominal pain, elevated LFTs) with areas of hemorrhage on gross examination.

**(Choice E)** Hydatid cysts are caused by the larvae form of *Echinococcus granulosus*, a canine tapeworm. This pathogen is rare in the United States, and hepatic echinococcal lesions would present as fluid-filled cysts lined by a membrane derived from the parasite.

### Educational objective:

Focal nodular hyperplasia is a benign liver tumor marked by a central stellate scar containing an abnormally large artery. It usually arises in young women and most cases are asymptomatic and found incidentally.

Pathology

Gastrointestinal &amp; Nutrition

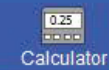
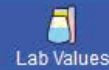
Focal nodular hyperplasia

Subject

System

Topic





A 45-year-old man comes to the office due to several months of diarrhea. The patient experiences watery diarrhea shortly after eating, occasional abdominal discomfort, easy fatigability, and unintentional weight loss. He has a history of Crohn disease for which he takes mesalamine. The patient also takes prednisone intermittently for disease exacerbations, and 6 months ago he was treated with metronidazole for a perianal abscess. Surgical history includes several intestinal resections due to complications of Crohn disease. He does not use tobacco or illicit drugs but drinks alcohol occasionally. Physical examination shows conjunctival pallor. The abdomen is nondistended, soft, and nontender. Vibratory and position sense are decreased in the lower extremities. Stool guaiac test is negative. Laboratory studies show macrocytic anemia and a low vitamin B<sub>12</sub> level. Which of the following is the most likely cause of this patient's presenting symptoms?

- ☐ A. Hormone-induced luminal secretion
- ☐ B. Infection with a protozoan parasite
- ☐ C. Infection with gram-positive, PAS-positive bacilli
- ☐ D. Loss of intestinal absorptive area
- ☐ E. Medication adverse effect





prednisone intermittently for disease exacerbations, and 6 months ago he was treated with metronidazole for a perianal abscess. Surgical history includes several intestinal resections due to complications of Crohn disease. He does not use tobacco or illicit drugs but drinks alcohol occasionally. Physical examination shows conjunctival pallor. The abdomen is nondistended, soft, and nontender. Vibratory and position sense are decreased in the lower extremities. Stool guaiac test is negative. Laboratory studies show macrocytic anemia and a low vitamin B<sub>12</sub> level. Which of the following is the most likely cause of this patient's presenting symptoms?

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- ☐ D. Loss of intestinal absorptive area
- ☐ E. Medication adverse effect
- ☐ F. Pancreatic enzyme deficiency
- ☐ G. Postprandial rapid fluid shifts







disease. He does not use tobacco or illicit drugs but drinks alcohol occasionally. Physical examination shows conjunctival pallor. The abdomen is nondistended, soft, and nontender. Vibratory and position sense are decreased in the lower extremities. Stool guaiac test is negative. Laboratory studies show macrocytic anemia and a low vitamin B<sub>12</sub> level. Which of the following is the most likely cause of this patient's presenting symptoms?

- ☐ A. Hormone-induced luminal secretion (0%)
- ☐ B. Infection with a protozoan parasite (2%)
- ☐ C. Infection with gram-positive, PAS-positive bacilli (2%)
- ☒ D. Loss of intestinal absorptive area (87%)
- ☐ E. Medication adverse effect (2%)
- ☐ F. Pancreatic enzyme deficiency (2%)
- ☐ G. Postprandial rapid fluid shifts (1%)

Correct

87%

01 min, 09 secs

11/21/2020

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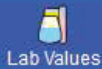
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Feedback

Suspend

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This patient likely has **short bowel syndrome**, a malabsorptive condition that typically occurs in patients with massive **small bowel resection** and/or **Crohn disease**. Extensive intestinal disease or resection results in loss of absorptive surface area and a decrease in intestinal transit time, leading to postprandial voluminous diarrhea and weight loss due to **malabsorption** of macro- and micronutrients.

Loss of functional distal ileum may specifically result in **vitamin B<sub>12</sub> deficiency** with macrocytic anemia, peripheral neuropathy, and subacute combined degeneration of the spinal cord (eg, impaired vibration and position sense).

**(Choice A)** VIPoma is a pancreatic neuroendocrine tumor that secretes vasoactive intestinal polypeptide, resulting in secretory watery diarrhea (persists with fasting) and flushing. Malabsorption of macro- and micronutrients is not characteristic.

**(Choice B)** Giardia is a protozoan parasite that may cause chronic diarrhea and malabsorption; however, infection typically occurs in high-risk individuals such as infants, campers/hikers drinking from mountain streams, those who are immunocompromised, and travelers to resource-limited areas.

**(Choice C)** Whipple disease is a rare multisystemic disorder caused by *Tropheryma whipplei*, a gram-positive, periodic acid-Schiff (PAS)-positive bacilli. Patients typically present with migratory polyarthrit





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice C)** Whipple disease is a rare multisystemic disorder caused by *Tropheryma whipplei*, a gram-positive, periodic acid-Schiff (PAS)-positive bacilli. Patients typically present with migratory polyarthritides followed by abdominal pain and malabsorptive diarrhea. Neurologic symptoms (eg, cognitive dysfunction, myoclonus) and cardiac disease (eg, endocarditis) are also characteristic.

**(Choice E)** Numerous medications can cause diarrhea as an adverse effect; however, this is unlikely in this patient with malabsorption, vitamin B<sub>12</sub> deficiency, and weight loss in the setting of Crohn disease and intestinal resection.

**(Choice F)** Chronic pancreatitis is most commonly caused by alcohol abuse and typically presents with abdominal pain and pancreatic insufficiency. Patients often have chronic diarrhea/malabsorption due to lack of digestive enzymes (exocrine insufficiency) and diabetes mellitus due to endocrine insufficiency.

**(Choice G)** Dumping syndrome may occur after gastric bypass surgery or damage to the pyloric sphincter. Emptying of hyperosmolar chyme into the small intestine causes a rapid shift of fluid from the serum to the intestine, resulting in postprandial gastrointestinal (eg, nausea/vomiting, cramps, diarrhea) and vasomotor symptoms (eg, diaphoresis, flushing).

### Educational objective:

Short bowel syndrome typically occurs in patients with massive small bowel resection and/or Crohn



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Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

this patient with malabsorption, vitamin B<sub>12</sub> deficiency, and weight loss in the setting of Crohn disease and intestinal resection.

**(Choice F)** Chronic pancreatitis is most commonly caused by alcohol abuse and typically presents with abdominal pain and pancreatic insufficiency. Patients often have chronic diarrhea/malabsorption due to lack of digestive enzymes (exocrine insufficiency) and diabetes mellitus due to endocrine insufficiency.

**(Choice G)** Dumping syndrome may occur after gastric bypass surgery or damage to the pyloric sphincter. Emptying of hyperosmolar chyme into the small intestine causes a rapid shift of fluid from the serum to the intestine, resulting in postprandial gastrointestinal (eg, nausea/vomiting, cramps, diarrhea) and vasomotor symptoms (eg, diaphoresis, flushing).

### Educational objective:

Short bowel syndrome typically occurs in patients with massive small bowel resection and/or Crohn disease due to loss of intestinal absorptive surface area and a decrease in intestinal transit time. Patients usually present with postprandial voluminous diarrhea and weight loss due to malabsorption. Loss of functional distal ileum may result in vitamin B<sub>12</sub> deficiency.

### References

- [Short bowel syndrome: a review of management options.](#)



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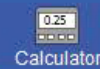
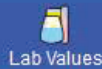
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A 34-year-old man comes to the office due to 2 days of anorexia, nausea, and dark-colored urine. He travels frequently for business and recently returned from a trip to Mexico. The patient has a history of asthma and occasionally uses inhaled albuterol for symptom management. His temperature is 37.8 C (100.2 F), blood pressure is 125/70 mm Hg, and pulse is 94/min. Cardiopulmonary examination is normal. There is mild right upper quadrant abdominal tenderness with no guarding or rebound. Serologic testing for *Entamoeba histolytica* is negative. Which of the following findings is most likely to be seen on liver biopsy in this patient?

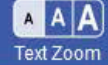
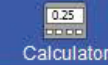
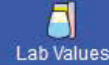
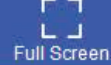
- ☐ A. Fibrinoid necrosis
- ☐ B. Hepatocyte swelling
- ☐ C. Liquefactive necrosis
- ☐ D. Malignant cells
- ☐ E. Regenerative nodules

**Submit**

Block Time Remaining: 00:23:27

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A 34-year-old man comes to the office due to 2 days of anorexia, nausea, and dark-colored urine. He travels frequently for business and recently returned from a trip to Mexico. The patient has a history of asthma and occasionally uses inhaled albuterol for symptom management. His temperature is 37.8 C (100.2 F), blood pressure is 125/70 mm Hg, and pulse is 94/min. Cardiopulmonary examination is normal. There is mild right upper quadrant abdominal tenderness with no guarding or rebound. Serologic testing for *Entamoeba histolytica* is negative. Which of the following findings is most likely to be seen on liver biopsy in this patient?

- ☐ A. Fibrinoid necrosis (6%)
- ☒ B. Hepatocyte swelling (80%)
- ☐ C. Liquefactive necrosis (5%)
- ☐ D. Malignant cells (1%)
- ☐ E. Regenerative nodules (6%)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient's presentation with low-grade fever, anorexia/nausea, dark-colored urine, and right upper quadrant abdominal tenderness is highly suggestive of **acute viral hepatitis**. Hepatitis A virus (HAV) is most likely responsible as it is the most common cause of acute viral hepatitis in young adults and this patient has just returned from an endemic region.

Although liver biopsy is not required to make the diagnosis, the hallmark histologic findings of acute viral hepatitis include hepatocyte necrosis and apoptosis with mononuclear infiltration. **Hepatocyte necrosis** is characterized by **cellular swelling** and **cytoplasmic emptying** (eg, "ballooning degeneration") likely caused by ATP depletion and disruption of the intermediate filament network. In severe cases, regions of adjacent lobules are interconnected by swaths of dead hepatocytes called "bridging necrosis." **Hepatocyte apoptosis** is characterized by **cellular shrinkage** and nuclear fragmentation with intense **eosinophilia** (eg, Councilman bodies) and is likely caused by mitochondrial oxidative damage. The presence of virally infected and dying hepatocytes promotes **mononuclear inflammation** in the sinusoids and portal tracts.

**(Choice A)** Fibrinoid necrosis is characterized by the deposition of amorphous, proteinaceous material in the walls of blood vessels affected by immune vasculitis or malignant hypertension.

**(Choice C)** Severe viral hepatitis can cause coagulative necrosis of hepatocytes. However, liquefactive



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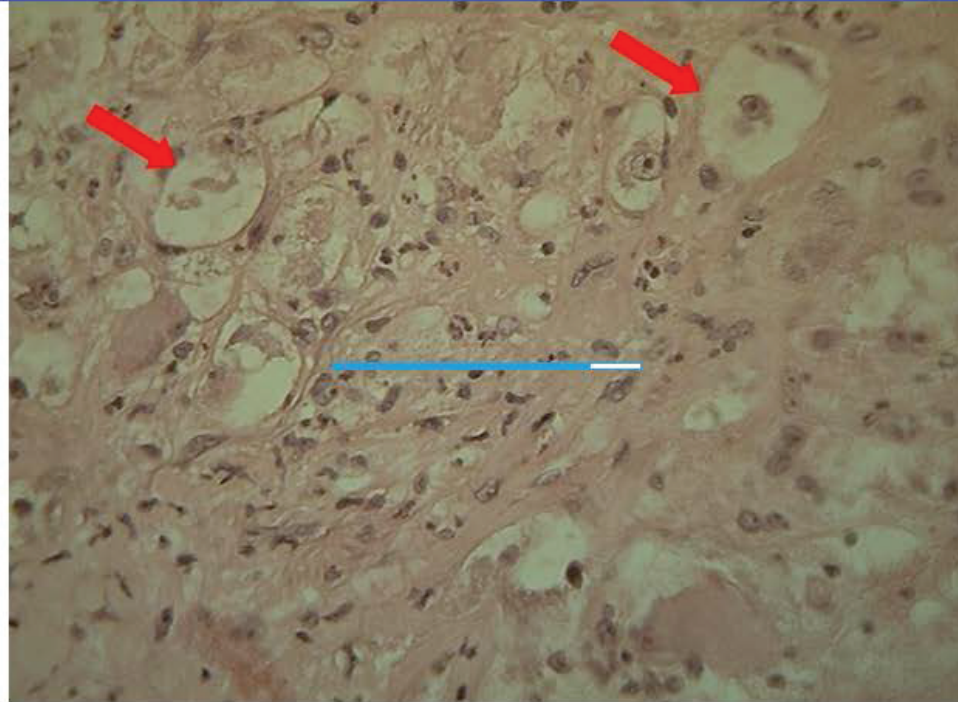


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Exhibit Display



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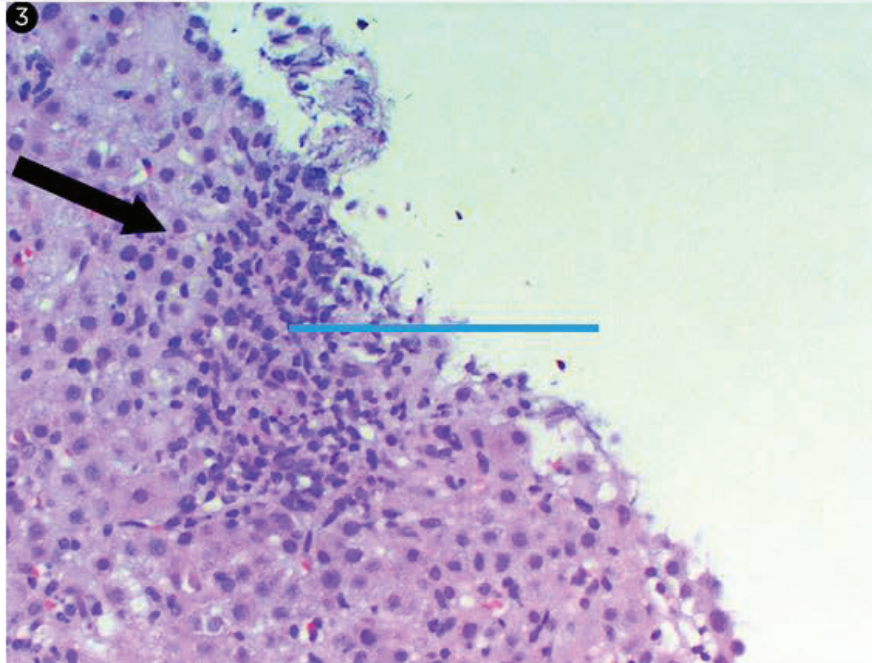
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Zoom In

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New | Existing

My Notebook





Mark



Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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Settings

the walls of blood vessels affected by immune vasculitis or malignant hypertension.

**(Choice C)** Severe viral hepatitis can cause coagulative necrosis of hepatocytes. However, liquefactive necrosis classically occurs in the central nervous system due to enzymatic degradation of tissue. Amebic liver abscesses caused by *Entamoeba histolytica* infection may also produce liquefactive necrosis, but this is unlikely in the setting of negative serologic testing.

**(Choice D)** HAV is not associated with an increased risk of hepatocellular cancer. However, hepatitis B and C infections, aflatoxin B exposure, and all other forms of chronic hepatocyte injury are associated with increased incidence of hepatocellular carcinoma.

**(Choice E)** Nodular regeneration of hepatocytes is generally found in patients with cirrhosis due to chronic hepatitis. HAV does not cause chronic hepatitis, but HBV and HCV are associated with chronic hepatitis that can result in cirrhosis.

### Educational objective:

Acute hepatitis due to most hepatotropic viruses causes hepatocyte ballooning degeneration and apoptosis with mononuclear cell infiltration.

### References

• Ballooned hepatocytes in acute hepatitis: the value of keratin immunohistochemistry for diagnosis



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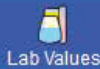
Feedback



Suspend



End Block



A 73-year-old woman is brought to the clinic by her niece due to a 10-day history of abdominal pain and loss of appetite. The patient does not like "going to the doctor" and has not been seen by a physician in many years. Frequent loose stools and loss of appetite have been present since the pain began. Family history is significant for colon cancer in a maternal aunt. Temperature is 37.8 C (100 F) and pulse is 98/min. Abdominal examination is significant for tenderness on deep palpation of the left lower quadrant, along with an appreciable mass. There is no inguinal lymphadenopathy. White blood cell count is 15,000/mm<sup>3</sup>. Which of the following is the most likely cause of the abdominal pain in this patient?

- ☐ A. Acute diverticulitis
- ☐ B. Colon cancer
- ☐ C. Incarcerated direct inguinal hernia
- ☐ D. Ischemic colitis
- ☐ E. Tubo-ovarian abscess
- ☐ F. Ulcerative colitis





loss of appetite. The patient does not like "going to the doctor" and has not been seen by a physician in many years. Frequent loose stools and loss of appetite have been present since the pain began. Family history is significant for colon cancer in a maternal aunt. Temperature is 37.8 C (100 F) and pulse is 98/min. Abdominal examination is significant for tenderness on deep palpation of the left lower quadrant, along with an appreciable mass. There is no inguinal lymphadenopathy. White blood cell count is 15,000/mm<sup>3</sup>. Which of the following is the most likely cause of the abdominal pain in this patient?

- ✓ ☒ A. Acute diverticulitis (66%)
- ☐ B. Colon cancer (14%)
- ☐ C. Incarcerated direct inguinal hernia (4%)
- ☐ D. Ischemic colitis (5%)
- ☐ E. Tubo-ovarian abscess (5%)
- ☐ F. Ulcerative colitis (2%)

Correct

66%



38 secs



02/07/2021

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Feedback



Suspend



End Block



### Acute diverticulitis

<b>Pathogenesis</b>	<ul style="list-style-type: none"> <li>Trapped food particles &amp; ↑ intracolonic pressure that cause microperforation of colonic diverticula</li> </ul>
<b>Clinical presentation</b>	<ul style="list-style-type: none"> <li>Abdominal pain (usually left lower quadrant)</li> <li>Nausea, vomiting, change in bowel habits</li> <li>Tenderness ± palpable mass</li> <li>Leukocytosis</li> </ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"> <li>Abdominal CT scan (oral &amp; intravenous contrast)</li> </ul>

This patient with abdominal pain, leukocytosis, low-grade fever, and a mass palpated in the left lower quadrant likely has acute diverticulitis. Diverticulitis is characterized by inflammation of colonic diverticula (ie, herniated outpouchings of the colonic mucosa and submucosa through the muscularis mucosae) and is caused by trapped food particles and elevated intraluminal pressure within a diverticulum, resulting in microperforation. The risk increases with age (particularly in those age ≥60).

Patients commonly present with constant **abdominal pain**, classically in the **left lower quadrant**, signifying sigmoid colon involvement. Other symptoms include nausea, vomiting, and changes in bowel



microperforation. The risk increases with age (particularly in those age  $\geq 60$ ).

Patients commonly present with constant **abdominal pain**, classically in the **left lower quadrant**, signifying sigmoid colon involvement. Other symptoms include nausea, vomiting, and changes in bowel habits (constipation or diarrhea). Patients often have low-grade **fever**, and examination may reveal **lower abdominal tenderness** and, often, a **palpable mass** due to inflammation or abscess formation. Mild leukocytosis is a common laboratory finding; occult blood may be present, but gross hematochezia is rare.

**(Choice B)** Colon cancer may present with abdominal pain. However, a tumor large enough to palpate on examination suggests extensive disease and would typically be associated with more chronic symptoms (eg, weight loss). The leukocytosis and short duration of symptoms in this patient are more consistent with diverticulitis.

**(Choice C)** Incarcerated direct inguinal hernias cause a palpable mass; however, the mass would typically be in the groin, not the abdomen. In addition, unless the hernia is strangulated, leukocytosis and fevers are unexpected.

**(Choice D)** Ischemic colitis is a common cause of abdominal pain in an older patient; however, it typically presents with hematochezia and postprandial pain in patients with ischemic risk factors (eg, hypertension, diabetes).





be in the groin, not the abdomen. In addition, unless the hernia is strangulated, leukocytosis and fevers are unexpected.

**(Choice D)** Ischemic colitis is a common cause of abdominal pain in an older patient; however, it typically presents with hematochezia and postprandial pain in patients with ischemic risk factors (eg, hypertension, diabetes).

**(Choice E)** Tubo-ovarian abscess can cause abdominal pain and leukocytosis; however, patients typically have vaginal discharge, and a mass (if present) is located in the pelvis, not the abdomen. Tubo-ovarian abscesses typically occur in the setting of pelvic inflammatory disease, which is far more common in patients age <40.

**(Choice F)** Ulcerative colitis often presents with abdominal pain and diarrhea; however, hematochezia is common. In addition, patients are typically diagnosed at age 20-40.

### Educational objective:

Diverticulitis is characterized by inflammation of colonic diverticula. Patients have abdominal pain, nausea, vomiting, and changes in bowel habits. Low-grade fever and leukocytosis are common, and physical examination may demonstrate a tender mass in the left lower quadrant.

### References







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 40-year-old female presented to the physician for evaluation of worsening fatigue. She has no other medical problems. She does not use tobacco, alcohol or drugs. Vital signs are within normal limits. Physical examination is within normal limits. Laboratory evaluation shows an alkaline phosphatase level of 180 U/L. Which of the following should be checked next?

- ☐ A. Unconjugated bilirubin level
- ☐ B. Lactate dehydrogenase level
- ☐ C. Serum ammonia levels
- ☐ D. Prothrombin time
- ☐ E.  $\gamma$ -glutamyl transpeptidase
- ☐ F. Aspartate aminotransferase

**Submit**

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Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 40-year-old female presented to the physician for evaluation of worsening fatigue. She has no other medical problems. She does not use tobacco, alcohol or drugs. Vital signs are within normal limits. Physical examination is within normal limits. Laboratory evaluation shows an alkaline phosphatase level of 180 U/L. Which of the following should be checked next?

- ☐ A. ~~Unconjugated bilirubin level~~ (18%)
- ☐ B. Lactate dehydrogenase level (11%)
- ☐ C. ~~Serum ammonia levels~~ (4%)
- ☐ D. ~~Prothrombin time~~ (6%)
- ☒ E.  $\gamma$ -glutamyl transpeptidase (42%)
- ☐ F. Aspartate aminotransferase (17%)

Correct

42%  
Answered correctly01 min, 26 secs  
Time Spent01/30/2021  
Last Updated

Block Time Remaining: 00:26:10

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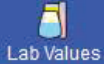
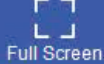
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Broadly speaking, laboratory tests used in the evaluation of hepatobiliary disease either assess liver functionality (eg, prothrombin time, bilirubin, albumin, cholesterol) or the structural integrity and cellular intactness of the liver (eg, transaminases) or the biliary tract (eg, alkaline phosphatase,  $\gamma$ -glutamyl transferase).

Alkaline phosphatase represents a group of enzymes associated with metabolic activity in a number of tissues, including liver, bone, intestine, kidney, placenta, leukocytes, and some neoplasms. Bone and liver are the primary sources of alkaline phosphatase, with threefold elevations considered a relatively nonspecific finding for many liver diseases. To clarify the importance of a moderately elevated alkaline phosphatase, the hepatic  $\gamma$ -glutamyl transpeptidase (GGTP) should be evaluated.

$\gamma$ -glutamyl transpeptidase is an enzyme predominantly present in hepatocytes and biliary epithelia. While it too can be found in various extrahepatic tissues (organs such as kidney, spleen, pancreas, heart, lung, and brain), GGTP is not present to a significant extent in bone. It is therefore particularly useful in determining whether an elevated alkaline phosphatase is of hepatic or bony origin.

**(Choice A)** Measurement of unconjugated bilirubin (especially in contrast to conjugated bilirubin) can be of assistance in distinguishing hemolytic conditions from hepatic dysfunction or bile duct obstruction. This test







whether an elevated alkaline phosphatase is of hepatic or bony origin.

**(Choice A)** Measurement of unconjugated bilirubin (especially in contrast to conjugated bilirubin) can be of assistance in distinguishing hemolytic conditions from hepatic dysfunction or bile duct obstruction. This test is not particularly helpful in following up an elevated alkaline phosphatase.

**(Choice B)** Lactate dehydrogenase is a relatively nonspecific test that can be of some assistance in the evaluation of tissue injury or death. It is not the most helpful test in following up an elevated alkaline phosphatase.

**(Choice C)** Serum ammonia levels can be of assistance in determining the extent of liver failure or gastrointestinal bleeding, among other conditions. It is not the most helpful test in following up an elevated alkaline phosphatase.

**(Choice D)** Prothrombin time is of assistance in assessing coagulative ability and liver functionality, especially in the acute setting. It is not the most helpful test in following up an elevated alkaline phosphatase.

**(Choice F)** Aspartate aminotransferase is of assistance in assessing and monitoring hepatic damage. It is not the most helpful test in following up an elevated alkaline phosphatase.

**Educational Objective:**





Mark



Previous



Next



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Lab Values



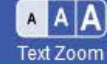
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Text Zoom



Settings

phosphatase.

**(Choice C)** Serum ammonia levels can be of assistance in determining the extent of liver failure or gastrointestinal bleeding, among other conditions. It is not the most helpful test in following up an elevated alkaline phosphatase.

**(Choice D)** Prothrombin time is of assistance in assessing coagulative ability and liver functionality, especially in the acute setting. It is not the most helpful test in following up an elevated alkaline phosphatase.

**(Choice F)** Aspartate aminotransferase is of assistance in assessing and monitoring hepatic damage. It is not the most helpful test in following up an elevated alkaline phosphatase.

### Educational Objective:

A moderately elevated alkaline phosphatase of unclear etiology should be followed up with  $\gamma$ -glutamyl transpeptidase.

Pathology

Gastrointestinal &amp; Nutrition

Abnormal lfts

Subject

System

Topic

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Previous



Next



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Notes



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Settings

A 55-year-old man with a history of chronic pancreatitis and alcohol abuse is investigated for recent onset weight loss, decreased appetite, and worsening of chronic abdominal pain. Physical examination is significant for diffuse muscle atrophy, temporal wasting, and a mildly enlarged liver without ascites. Serum lipase and amylase are normal, and aspartate aminotransferase (AST) is mildly elevated. Abdominal imaging shows a malignant mass in the pancreas. The patient subsequently undergoes an uncomplicated subtotal pancreatectomy and returns for a postoperative nutritional assessment following hospital discharge. Which of the following tests will most likely be normal in this patient after surgery?

- ☐ A. Duodenal lipase levels after cholecystokinin stimulation
- ☐ B. Duodenal trypsin levels after cholecystokinin stimulation
- ☐ C. Intestinal D-xylose absorption
- ☐ D. Serum trypsinogen
- ☐ E. Stool neutral fat content

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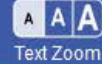
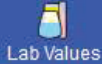
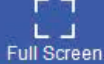


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A 55-year-old man with a history of **chronic pancreatitis** and alcohol abuse is investigated for recent onset weight loss, decreased appetite, and worsening of chronic abdominal pain. Physical examination is significant for diffuse muscle atrophy, temporal wasting, and a mildly enlarged liver without ascites. Serum lipase and amylase are normal, and aspartate aminotransferase (AST) is mildly elevated. Abdominal imaging shows a malignant mass in the pancreas. The patient subsequently undergoes an uncomplicated subtotal **pancreatectomy** and returns for a postoperative nutritional assessment following hospital discharge. Which of the following tests will most likely be normal in this patient after surgery?

- ☐ A. Duodenal lipase levels after cholecystokinin stimulation (6%)
- ☐ B. Duodenal trypsin levels after cholecystokinin stimulation (7%)
- ☒ C. Intestinal D-xylose absorption (68%)
- ☐ D. Serum trypsinogen (10%)
- ☐ E. Stool neutral fat content (6%)



The exocrine pancreas has a significant **secretory reserve**, and  $\geq 90\%$  of the glandular tissue must be destroyed before a patient will develop clinical malabsorption. However, this patient likely has significant loss of pancreatic tissue at baseline due to chronic pancreatitis and is at increased risk for **exocrine insufficiency**. Following partial pancreatic resection, he may develop clinically significant deficiency in any of the pancreatic digestive enzymes normally secreted into the duodenum.

Pancreatic amylases, along with salivary and brush border amylases, are required for the degradation of polysaccharides into monosaccharides, as polysaccharides cannot be absorbed by the intestinal mucosa. In contrast, **monosaccharides** (eg, glucose, galactose) are taken up directly by the epithelial cells of the small intestine through either sodium-dependent cotransport or facilitated diffusion. **D-xylose** is a monosaccharide that is absorbed directly without the action of pancreatic enzymes, and can be used to test for brush border absorptive function independent of pancreatic function. Intestinal D-xylose absorption can also decrease with bacterial overgrowth of the small intestine.

**(Choices A and B)** Patients with exocrine pancreatic insufficiency will have decreased secretion of trypsin and lipase into the duodenum following cholecystokinin (CCK) stimulation.

**(Choice D)** Trypsinogen is a proenzyme secreted by the exocrine pancreas into the small intestine. Small





also decrease with bacterial overgrowth of the small intestine.

**(Choices A and B)** Patients with exocrine pancreatic insufficiency will have decreased secretion of trypsin and lipase into the duodenum following cholecystokinin (CCK) stimulation.

**(Choice D)** Trypsinogen is a proenzyme secreted by the exocrine pancreas into the small intestine. Small quantities are also detectable in serum. Serum trypsinogen levels are increased in acute pancreatitis but often decreased in patients with chronic pancreatitis or other forms of chronic pancreatic insufficiency.

**(Choice E)** The stool neutral fat (triglyceride) content is increased after pancreatic resection due to deficiency of pancreatic lipase.

### Educational objective:

Polysaccharides must be degraded to monosaccharides by pancreatic and brush border amylases before they can be absorbed. Monosaccharides can be absorbed directly. D-xylose is a monosaccharide whose absorption is not affected by exocrine pancreatic insufficiency, and can be used to differentiate between pancreatic versus mucosal causes of malabsorption.

Pathophysiology

Gastrointestinal &amp; Nutrition

Malabsorption

Subject

System

Topic







A 50-year-old woman comes to the office for a preventive examination. She feels well and has no ongoing symptoms. Medical and family histories are unremarkable. The patient does not use tobacco or alcohol. Blood pressure is 132/76 mm Hg and pulse is 72/min. BMI is 25 kg/m<sup>2</sup>. Physical examination is normal. The patient is up to date on breast and cervical screening but has not undergone colon cancer screening. She is referred for colonoscopy, during which a single colon polyp is discovered. The polyp is removed and sent for histologic analysis. Which of the following pathologic findings is associated with the greatest risk of malignant transformation in this patient?

- ☐ A. 1-cm sessile hyperplastic polyp
- ☐ B. 2-cm sessile lymphoid polyp
- ☐ C. 2-cm tubular adenomatous polyp
- ☐ D. 2-cm villous adenomatous polyp
- ☐ E. 3-cm pedunculated hamartomatous polyp

**Submit**



Previous



Next



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Tutorial



Lab Values



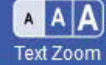
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Settings

A 50-year-old woman comes to the office for a preventive examination. She feels well and has no ongoing symptoms. Medical and family histories are unremarkable. The patient does not use tobacco or alcohol. Blood pressure is 132/76 mm Hg and pulse is 72/min. BMI is 25 kg/m<sup>2</sup>. Physical examination is normal. The patient is up to date on breast and cervical screening but has not undergone colon cancer screening. She is referred for colonoscopy, during which a single colon polyp is discovered. The polyp is removed and sent for histologic analysis. Which of the following pathologic findings is associated with the greatest risk of malignant transformation in this patient?

- ☐ A. 1-cm sessile hyperplastic polyp (5%)
- ☐ B. 2-cm sessile lymphoid polyp (3%)
- ☐ C. 2-cm tubular adenomatous polyp (3%)
- ☒ D. 2-cm villous adenomatous polyp (85%)
- ☐ E. 3-cm pedunculated hamartomatous polyp (2%)



1



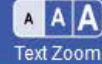
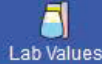
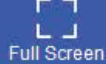
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Common colonic polyps	
Neoplastic	Non-neoplastic
<ul style="list-style-type: none"><li>• Serrated</li><li>• Adenomatous (villous &gt; tubular)</li></ul>	<ul style="list-style-type: none"><li>• Hyperplastic</li><li>• Inflammatory</li><li>• Juvenile</li><li>• Submucosal</li></ul>

Colonic polyps may be differentiated as non-neoplastic and neoplastic. Most are non-neoplastic and do not increase the risk of colon adenocarcinoma; such types include:

1. **Hyperplastic polyps**, the most common non-neoplastic polyp, are typically small and composed of well-differentiated mucosal cells that form glands and crypts (**Choice A**).
2. Inflammatory polyps, seen in ulcerative colitis and Crohn disease, are composed of regenerating intestinal mucosa and inflammatory cells.
3. Submucosal polyps, are typically composed of lipomas or lymphoid aggregates that bulge up into the mucosa (**Choice B**).







Mark



Previous



Next



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Notes



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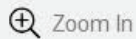
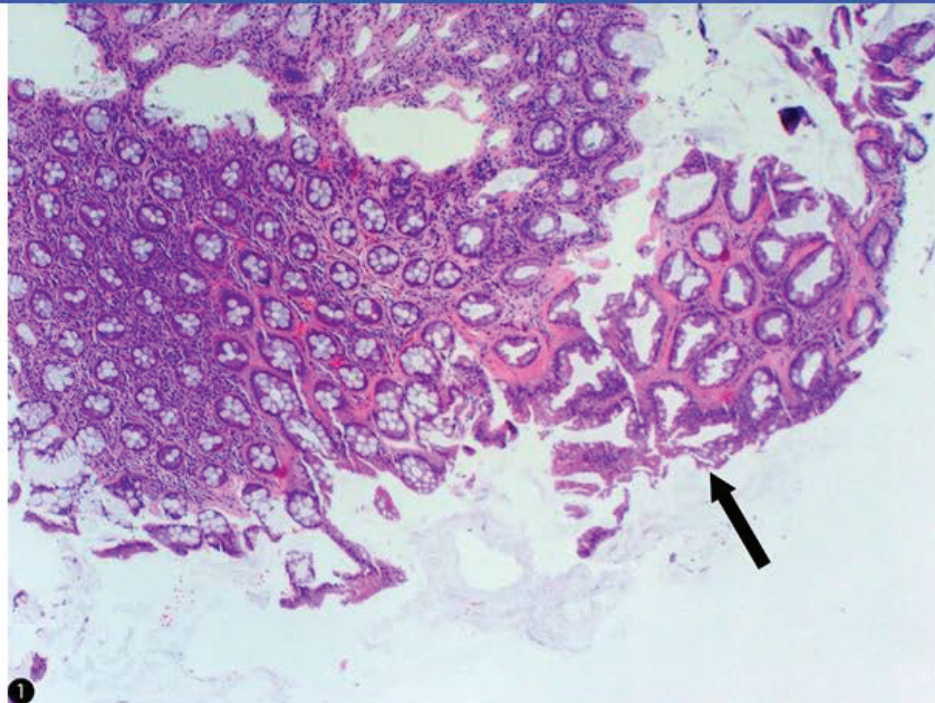


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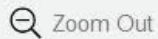


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## Exhibit Display



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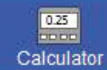
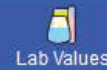
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mucosa (Choice B).

Neoplastic polyps include **adenomatous polyps** (ie, tubular, villous, tubulovillous) and **serrated polyps** (ie, sessile serrated polyp, traditional serrated adenoma). These polyps have the potential to transform into colonic adenocarcinoma. **Increasing polyp size** is the most important characteristic that **correlates with malignancy risk**; the risk is increased in polyps >10 mm and is greatest in those >4 cm. Other risk factors include degree of dysplasia and histologic pattern. **Villous adenomas** are more likely to undergo malignant transformation than **tubular adenomas** (Choice C).

**(Choice E)** Hamartomatous polyps consist of disorganized mucosal glands, smooth muscle, and connective tissue. **Sporadic juvenile polyps** are solitary hamartomatous lesions that are not associated with increased risk of colon cancer. Multiple hamartomatous polyps frequently occur in Peutz-Jeghers and juvenile polyposis syndromes, both of which confer an increased risk of malignancy.

### Educational objective:

Adenomatous and serrated polyps (ie, sessile serrated polyp, traditional serrated adenoma) are neoplastic polyps that have malignancy potential. Increasing polyp size is the most important risk factor for cancer; villous histology and high-grade dysplasia are additional risk factors.

Pathology

Gastrointestinal &amp; Nutrition

Colorectal polyps and cancer

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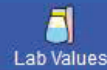
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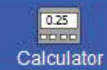
Tutorial



Lab Values



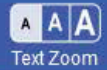
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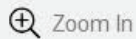
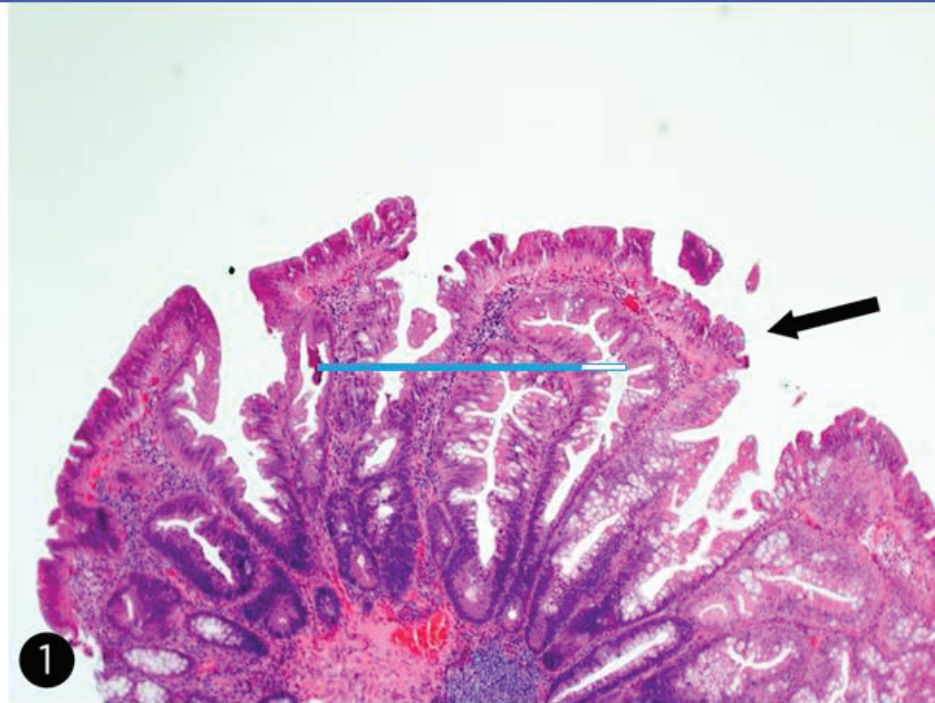
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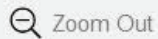
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Mucosa (Choice B).

Exhibit Display



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Block Time Remaining: 00:27:33

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Lab Values



Notes



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Text Zoom

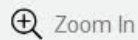
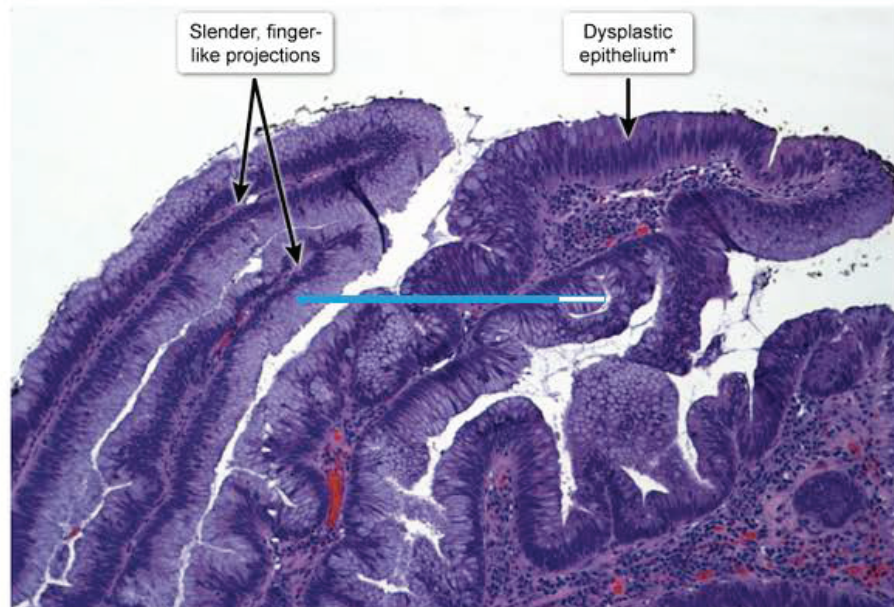


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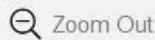
mucosa (choice B).

## Exhibit Display

## Colonic villous adenoma



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Feedback



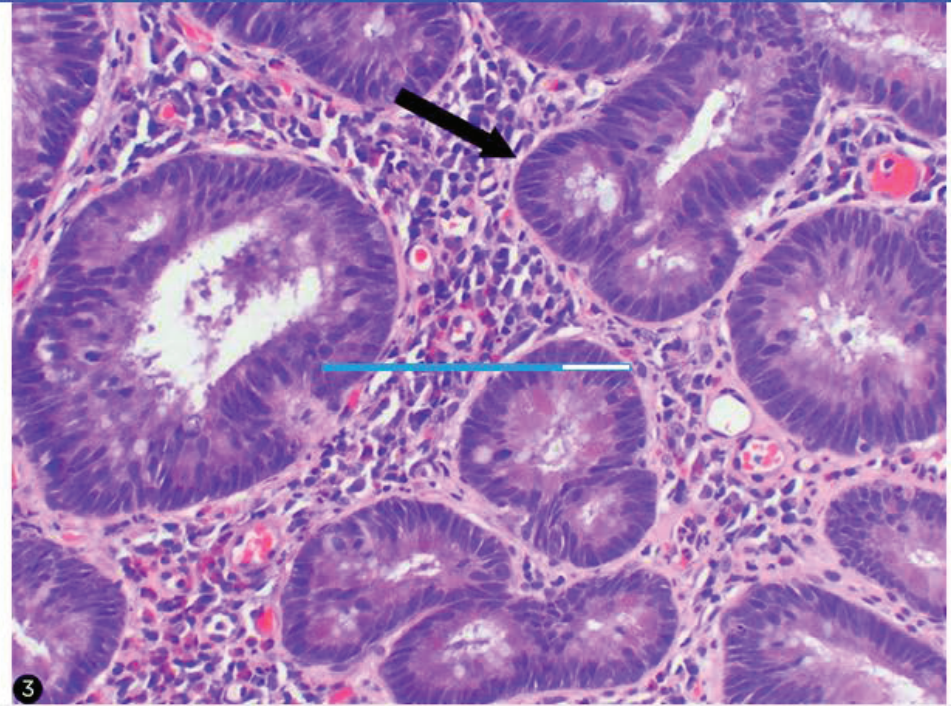
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End Block

Mucosa (Choice B).

Exhibit Display



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Tutorial



Lab Values



Notes



Calculator



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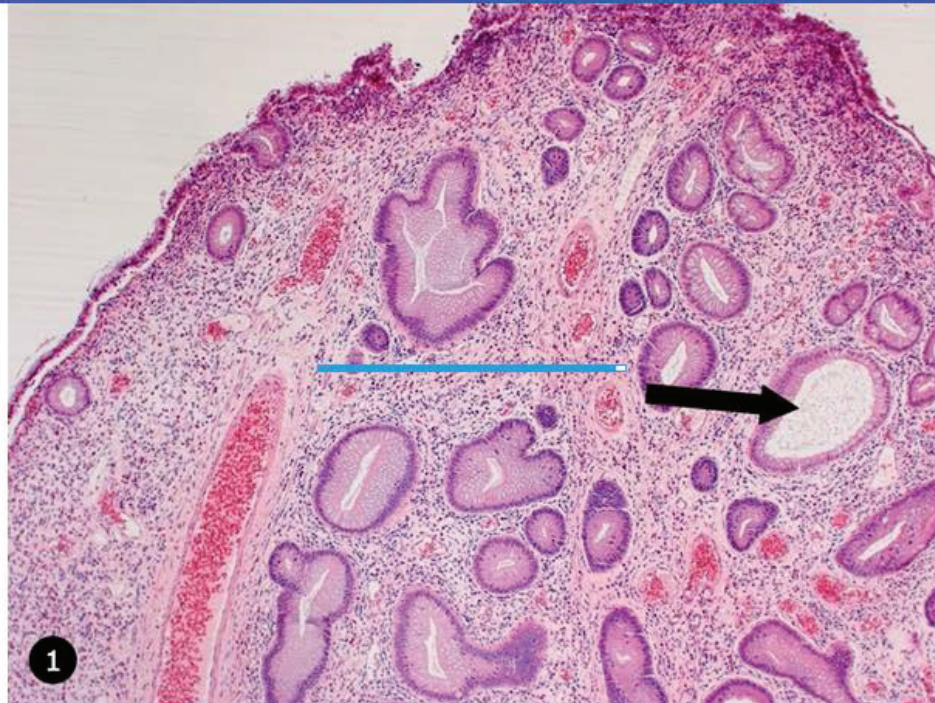
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mucosa (choice B).

## Exhibit Display



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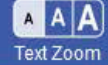
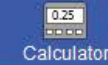
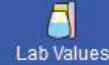
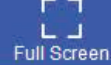


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A 65-year-old man comes to the office due to progressive weight loss, jaundice, and anorexia over the last 3 months. His urine has been dark and his stools have been pale. The patient has no prior medical conditions and takes no medications. He has smoked a pack of cigarettes a day for 40 years. He drinks 2 cups of coffee every day and 1 or 2 glasses of wine on most nights. He used illicit drugs for 2 years when he was in his teens but has used none since. The patient has a sedentary lifestyle and frequently consumes red and processed meats. Vital signs are within normal limits. BMI is 28 kg/m<sup>2</sup>. Physical examination shows scleral icterus. The chest is clear to auscultation and percussion. Abdominal examination shows an enlarged but nontender gallbladder. There is no ascites. Which of the following is the strongest factor predisposing to this patient's current condition?

- ☐ A. Alcohol use
- ☐ B. Cigarette smoking
- ☐ C. Coffee consumption
- ☐ D. Low-fiber diet
- ☐ E. Processed meat consumption





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

3 months. His urine has been dark and his stools have been pale. The patient has no prior medical conditions and takes no medications. He has smoked a pack of cigarettes a day for 40 years. He drinks 2 cups of coffee every day and 1 or 2 glasses of wine on most nights. He used illicit drugs for 2 years when he was in his teens but has used none since. The patient has a sedentary lifestyle and frequently consumes red and processed meats. Vital signs are within normal limits. BMI is 28 kg/m<sup>2</sup>. Physical examination shows scleral icterus. The chest is clear to auscultation and percussion. Abdominal examination shows an enlarged but nontender gallbladder. There is no ascites. Which of the following is the strongest factor predisposing to this patient's current condition?

- ☐ A. Alcohol use
- ☐ B. Cigarette smoking
- ☐ C. Coffee consumption
- ☐ D. Low-fiber diet
- ☐ E. Processed meat consumption
- ☐ F. Viral hepatitis



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

cups of coffee every day and 1 or 2 glasses of wine on most nights. He used illicit drugs for 2 years when he was in his teens but has used none since. The patient has a sedentary lifestyle and frequently consumes red and processed meats. Vital signs are within normal limits. BMI is 28 kg/m<sup>2</sup>. Physical examination shows scleral icterus. The chest is clear to auscultation and percussion. Abdominal examination shows an enlarged but nontender gallbladder. There is no ascites. Which of the following is the strongest factor predisposing to this patient's current condition?

- ☐ A. Alcohol use (18%)
- ☒ B. Cigarette smoking (44%)
- ☐ C. Coffee consumption (0%)
- ☐ D. Low-fiber diet (3%)
- ☐ E. Processed meat consumption (9%)
- ☐ F. Viral hepatitis (23%)

Correct

44%



01 min, 04 secs



10/10/2020

Block Time Remaining: 00:28:37

TUTOR

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Pancreatic adenocarcinoma

#### Risk factors

- Age  $\geq 65$
- Smoking
- Chronic pancreatitis
- Genetic predisposition
  - Hereditary pancreatitis
  - Peutz-Jeghers syndrome
  - MEN syndromes
  - Hereditary nonpolyposis colon cancer

#### Clinical presentation

- Weight loss, anorexia
- Abdominal/back pain or painless obstructive jaundice
- Migratory thrombophlebitis
- Hepatomegaly & ascites (with metastasis)

**Pancreatic adenocarcinoma** should be considered in any patient with painless **obstructive jaundice**



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

- Hepatomegaly & ascites (with metastasis)

**Pancreatic adenocarcinoma** should be considered in any patient with painless **obstructive jaundice** (elevated bilirubin, dark urine, pale stools) and **weight loss**. Courvoisier sign (painless palpable gallbladder in a jaundiced patient) can also raise suspicion, although this can be seen in a number of conditions (eg, cholangiocarcinoma, hepatic duct obstruction). Symptoms of pancreatic malignancy vary with location; tumors at the pancreatic head typically produce obstructive symptoms due to compression of the common bile duct (CBD), whereas those in the body and tail do not obstruct the CBD and often produce midepigastria pain due to invasion of the splanchnic plexus.

**Smoking** is the most important environmental risk factor for pancreatic cancer and doubles the risk.

**(Choice A)** Alcohol consumption increases the risk of malignant tumors involving the head, neck, esophagus, and liver. Chronic alcohol consumption can cause chronic pancreatitis, but moderate alcohol use in the absence of chronic pancreatitis does not appear to confer any additional risk for pancreatic cancer.

**(Choice C)** Chronic, heavy intake of hot beverages is associated with increased risk for esophageal cancer, but coffee intake does not increase the risk of pancreatic cancer.



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** Alcohol consumption increases the risk of malignant tumors involving the head, neck, esophagus, and liver. Chronic alcohol consumption can cause chronic pancreatitis, but moderate alcohol use in the absence of chronic pancreatitis does not appear to confer any additional risk for pancreatic cancer.

**(Choice C)** Chronic, heavy intake of hot beverages is associated with increased risk for esophageal cancer, but coffee intake does not increase the risk of pancreatic cancer.

**(Choices D and E)** A low-fiber diet and diets high in processed meats are associated with an increased risk of colon adenocarcinoma.

**(Choice F)** Chronic viral hepatitis B and C greatly increase the risk of hepatocellular carcinoma. They may increase the risk of pancreatic cancer, but only slightly.

### Educational objective:

Smoking is the most important environmental risk factor for pancreatic cancer. Other risk factors include advanced age, chronic pancreatitis, and genetic predisposition (eg, Peutz-Jeghers syndrome).

### References

- Alcohol intake and pancreatic cancer: A pooled analysis from the pancreatic cancer cohort consortium (PanScan).

Block Time Remaining: 00:28:37

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 46-year-old woman comes to the office with persistent diarrhea, weight loss, and abdominal pain. Her diarrhea started several months ago. She has no fever, melena, or hematochezia. The patient has not traveled outside of the country and has not drunk from any untreated freshwater sources. She has had no recent hospitalizations or antibiotic use. Her sister has a history of celiac disease. Upper endoscopy reveals postbulbar duodenal and jejunal ulcers. This patient most likely has a tumor secreting which of the following molecules?

- ☐ A. Gastrin
- ☐ B. Glucagon
- ☐ C. Insulin
- ☐ D. Serotonin
- ☐ E. Somatostatin
- ☐ F. Vasoactive intestinal polypeptide

**Submit**

Block Time Remaining: 00:28:39

TUTOR

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



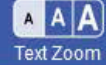
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Calculator



Reverse Color



Text Zoom



Settings

A 46-year-old woman comes to the office with persistent diarrhea, weight loss, and abdominal pain. Her diarrhea started several months ago. She has no fever, melena, or hematochezia. The patient has not traveled outside of the country and has not drunk from any untreated freshwater sources. She has had no recent hospitalizations or antibiotic use. Her sister has a history of celiac disease. Upper endoscopy reveals postbulbar duodenal and jejunal ulcers. This patient most likely has a tumor secreting which of the following molecules?

- ☒ A. Gastrin (73%)
- ☐ B. Glucagon (0%)
- ☐ C. Insulin (0%)
- ☐ D. Serotonin (3%)
- ☐ E. Somatostatin (1%)
- ☐ F. Vasoactive intestinal polypeptide (20%)



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



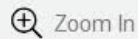
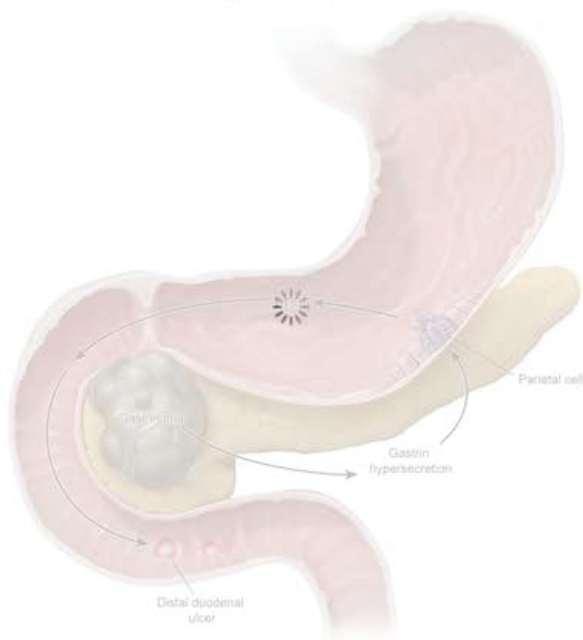
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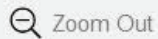
Settings

## Exhibit Display

## Zollinger-Ellison syndrome



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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This patient's clinical presentation is highly suggestive of **Zollinger-Ellison syndrome (ZES)**. ZES is caused by gastrin-secreting neuroendocrine tumors (**gastrinomas**) that are most commonly located in the small intestine or pancreas. The gastrin produced by these tumors stimulates gastric acid production, often resulting in multiple **peptic ulcers** that can be located **beyond the duodenal bulb** and are often refractory to therapy. Patients typically experience **abdominal pain** and acid reflux. They may also have **diarrhea** as gastric acid damages intestinal epithelial cells and inactivates pancreatic enzymes, preventing proper nutrient absorption.

The diagnosis of gastrinoma is made by measuring basal and stimulated gastrin levels (secretin stimulation test). Patients with ZES should undergo testing (eg, serum calcium, prolactin level) to exclude **multiple endocrine neoplasia type 1** due to the strong association between these conditions.

**(Choice B)** Glucagonomas are rare pancreatic alpha-cell tumors that present with diabetes mellitus and a raised erythematous rash that typically affects the groin (necrolytic migratory erythema).

**(Choice C)** Insulinomas are pancreatic beta-cell tumors that secrete insulin autonomously, regardless of blood glucose levels. As a result, patients usually have high circulating insulin/C-peptide levels and symptoms of hypoglycemia (eg, tremor, confusion).



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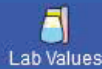
Feedback



Suspend



End Block



**(Choice C)** Insulinomas are pancreatic beta-cell tumors that secrete insulin autonomously, regardless of blood glucose levels. As a result, patients usually have high circulating insulin/C-peptide levels and symptoms of hypoglycemia (eg, tremor, confusion).

**(Choice D)** Carcinoid syndrome is most frequently caused by neuroendocrine tumors originating in the small intestine that have metastasized to the liver. These tumors secrete products such as serotonin and bradykinin, resulting in diarrhea, episodic flushing, right-sided valvular heart disease, and wheezing.

**(Choice E)** Somatostatinomas are rare tumors of the pancreatic D cells that present with diabetes mellitus (diminished insulin secretion), cholelithiasis (inhibition of cholecystokinin release), and diarrhea/steatorrhea (inhibition of pancreatic enzyme/bicarbonate secretion).

**(Choice F)** Vasoactive intestinal polypeptide is secreted by VIPomas, rare neuroendocrine tumors of the pancreas. Patients typically have diarrhea that persists with fasting, achlorhydria, and hypokalemia.

**Educational objective:**

Zollinger-Ellison syndrome is caused by gastrin-secreting tumors (gastrinomas) involving the small intestine or pancreas. Patients typically have peptic ulcers (often beyond the duodenal bulb), abdominal pain/acid reflux, and diarrhea. The condition is frequently associated with multiple endocrine neoplasia type 1.

**References**





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 53-year-old man comes to the physician with progressively worsening anorexia and abdominal discomfort. He has lost 14 kg (31 lb) since the onset of his symptoms about 4 months ago. Physical examination demonstrates nontender hepatomegaly. Laboratory studies show an elevated serum alkaline phosphatase level and a marginally elevated alanine aminotransferase level. A CT scan of the abdomen with oral and intravenous contrast is shown below.



0



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the most likely diagnosis?

- ☐ A. Hepatic adenoma
- ☐ B. Hepatic angiosarcoma
- ☐ C. Hepatoblastoma
- ☐ D. Hepatocellular carcinoma
- ☐ E. Intrahepatic cholangiocarcinoma
- ☐ F. Metastatic liver disease

Submit

Block Time Remaining: 00:29:20

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the most likely diagnosis?

- ☐ A. Hepatic adenoma (1%)
- ☐ B. Hepatic angiosarcoma (3%)
- ☐ C. Hepatoblastoma (0%)
- ☐ D. Hepatocellular carcinoma (9%)
- ☐ E. Intrahepatic cholangiocarcinoma (13%)
- ☒ F. Metastatic liver disease (71%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



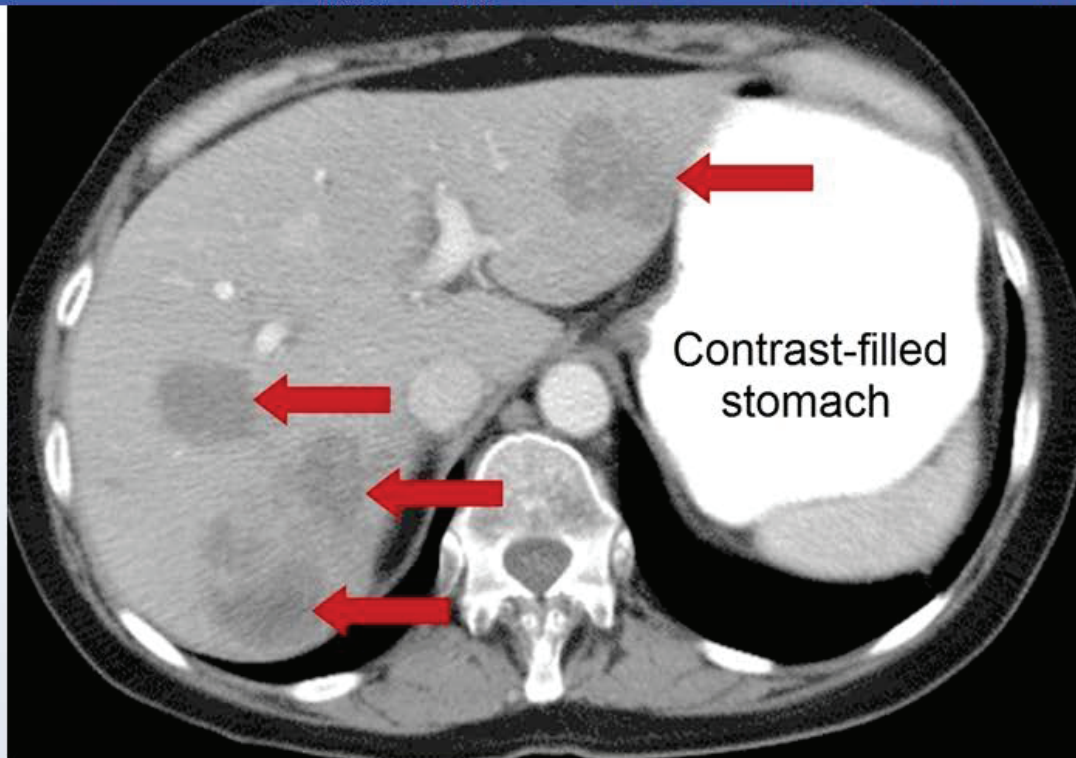
Reverse Color



Text Zoom



Settings



The patient's contrast-enhanced CT scan shows **multiple hypodense masses** in the liver (arrows) consistent with **metastatic liver disease**. Metastases are the most common malignant neoplasms of the

Block Time Remaining: 00:29:23

TUTOR

<https://t.me/USMLEWorldStep1>

0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The patient's contrast-enhanced CT scan shows **multiple hypodense masses** in the liver (arrows) consistent with **metastatic liver disease**. Metastases are the most common malignant neoplasms of the adult liver and are 20 times more common than hepatocellular carcinoma. The liver is the second most common site of metastatic spread (after the lymph nodes) because of its large size, dual blood supply, high perfusion rate, and the filtration function of Kupffer cells.

Patients with liver metastases typically have multiple nodules throughout the liver that may replace more than 80% of the hepatic parenchyma, often resulting in marked **hepatomegaly**. The nodules frequently outgrow their vascular supply and become centrally necrotic and umbilicated. Even with significant metastatic involvement, patients may have no clinical or laboratory signs suggestive of hepatic insufficiency. However, once the majority of the liver parenchyma is destroyed or the major bile ducts become obstructed with tumor, patients tend to present with jaundice or **abnormal hepatic enzymes** (eg, elevated aminotransferases, alkaline phosphatase).

**(Choice A)** Hepatic adenomas are uncommon, benign epithelial tumors of the liver that usually arise as a solitary mass in the right hepatic lobe. They are strongly associated with the use of oral contraceptives and anabolic steroids and are usually diagnosed in patients with upper abdominal pain or detected incidentally on imaging studies. They may rupture and cause intraabdominal hemorrhage.



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

on imaging studies. They may rupture and cause intraabdominal hemorrhage.

**(Choice B)** Hepatic angiosarcomas are associated with recent or remote exposure to vinyl chloride, arsenic, or Thorotrast. This tumor is extremely aggressive and is associated with a poor prognosis, as most patients die within a year.

**(Choice C)** Hepatoblastoma is the most common liver neoplasm of children and is associated with familial adenomatous polyposis and Beckwith-Wiedemann syndromes. This neoplasm is usually fatal within a few years if not surgically resected.

**(Choice D)** Hepatocellular carcinoma can present unifocally, multifocally, or as a diffusely infiltrative cancer. It is more common in older patients with a history of cirrhosis or infection with hepatitis B or C.

**(Choice E)** Cholangiocarcinoma is a rare malignancy that arises from the intra- and extrahepatic bile ducts. Intrahepatic cholangiocarcinoma appears grossly as a treelike mass that grows along the biliary system, typically resulting in extensive intrahepatic metastasis. Risk factors include primary sclerosing cholangitis, fibropolycystic liver disease, and infection with liver flukes in endemic areas. The prognosis is very poor.

### Educational objective:

Malignant hepatic lesions most often represent metastasis from another primary site (e.g., breast, lung).

Block Time Remaining: 00:29:23

TUTOR

<https://t.me/USMLEWorldStep1>



Feedback

Suspend

End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

adenomatous polyposis and Beckwith-Wiedemann syndromes. This neoplasm is usually fatal within a few years if not surgically resected.

**(Choice D)** Hepatocellular carcinoma can present unifocally, multifocally, or as a diffusely infiltrative cancer. It is more common in older patients with a history of cirrhosis or infection with hepatitis B or C.

**(Choice E)** Cholangiocarcinoma is a rare malignancy that arises from the intra- and extrahepatic bile ducts. Intrahepatic cholangiocarcinoma appears grossly as a treelike mass that grows along the biliary system, typically resulting in extensive intrahepatic metastasis. Risk factors include primary sclerosing cholangitis, fibropolycystic liver disease, and infection with liver flukes in endemic areas. The prognosis is very poor.

### Educational objective:

Malignant hepatic lesions most often represent metastasis from another primary site (eg, breast, lung, colon); primary liver neoplasms (eg, hepatocellular carcinoma) are much less common.

Pathology

Gastrointestinal &amp; Nutrition

Metastatic liver disease

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 34-year-old immigrant from southern Asia complains of intermittent abdominal cramps. He has had multiple respiratory infections over the last 2 years as well as a persistent, chronic cough. Laboratory results are as follows:

Complete blood count

Hemoglobin 13.0 g/dL

Leukocytes 6,800  
cells/ $\mu$ L

Neutrophils 56%

Eosinophils 14%

Lymphocytes 26%

Monocytes 4%

Which of the following findings in this patient would be most suggestive of *Strongyloides stercoralis* infection?



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Eosinophils 14%

Lymphocytes 26%

Monocytes 4%

Which of the following findings in this patient would be most suggestive of *Strongyloides stercoralis* infection?

- ☐ A. Parasite eggs in the stool
- ☐ B. Perianal egg deposition
- ☐ C. Proglottids in the stool
- ☐ D. Rhabditiform larvae in the stool
- ☐ E. Trophozoites and cysts in the stool

**Submit**



Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Neutrophils 56%  
Eosinophils 14%  
Lymphocytes 26%  
Monocytes 4%

Which of the following findings in this patient would be most suggestive of *Strongyloides stercoralis* infection?

- ☐ A. Parasite eggs in the stool (33%)
- ☐ B. Perianal egg deposition (6%)
- ☐ C. Proglottids in the stool (11%)
- ☒ D. Rhabditiform larvae in the stool (34%)
- ☐ E. Trophozoites and cysts in the stool (13%)

Correct



34%

Answered correctly



14 secs

Time spent



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Last updated



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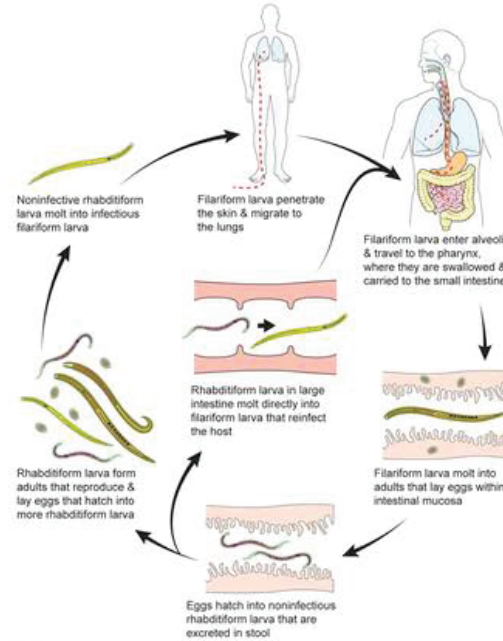


End Block



### Exhibit Display

#### Life cycle of *Strongyloides stercoralis*





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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Strongyloidiasis is a disease caused by the roundworm *Strongyloides stercoralis*. The infection is transmitted by filariform (infectious) larvae found in soil contaminated with human feces. On contact, the larvae **penetrate the skin** and migrate hematogenously to the lungs. There they enter the alveoli and travel up the bronchial tree to the pharynx, where they are swallowed. When the larvae reach the intestine, they develop into adults that lay eggs within the intestinal mucosa. These hatch into rhabditiform (noninfectious) larvae that migrate into the intestinal lumen to be excreted in the stool.

Some rhabditiform larvae can molt directly into filariform larva within the intestine and re-infect the host by penetrating the intestinal wall or perianal skin. This cycle of **autoinfection** can result in a massive increase in worm burden, leading to widespread dissemination of the parasites throughout the body (**hyperinfection**). The ensuing inflammation can be severe enough to cause multiorgan dysfunction and septic shock. Hyperinfection occurs most often in patients taking immunosuppressants (eg, corticosteroids) or with HTLV-1 infection. These patients have impaired  $T_H2$ -directed cellular immunity (mediated by the antihelminthic action of eosinophils and basophils).

Strongyloidiasis occurs most commonly in tropical and warm temperate regions, particularly Southeast Asia. Most patients are asymptomatic, but some present with chronic, intermittent gastrointestinal or pulmonary symptoms. Pruritic, erythematous, linear streaks (known as **larva currens**) may occur on the



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Strongyloidiasis occurs most commonly in tropical and warm temperate regions, particularly Southeast Asia. Most patients are asymptomatic, but some present with chronic, intermittent gastrointestinal or pulmonary symptoms. Pruritic, erythematous, linear streaks (known as **larva currens**) may occur on the thighs and buttocks as the larva migrate subcutaneously away from the perianal region. The diagnosis is made by finding rhabditiform **larvae in the stool**, as the **eggs and adult parasites** are usually seen only in intestinal biopsies. Treatment is with **ivermectin**.

**(Choice A)** Detection of parasite eggs in the stool is used to diagnose schistosomiasis caused by *Schistosoma mansoni* or *S japonicum*. *S stercoralis* eggs typically hatch within the intestinal mucosa and are not found in stool.

**(Choice B)** *Enterobius vermicularis* (pinworms) migrate out of the anus at night to deposit eggs on the surrounding perianal folds. **Pinworm eggs** are best detected by examining a piece of scotch tape applied to the perianal region shortly after awakening.

**(Choice C)** Intestinal tapeworms (eg, *Taenia solium*, *T saginata*, *Diphyllobothrium latum*) are flatworms made up of multiple segments called proglottids. These are shed from the distal end of the worm and can be detected in the stool of infected individuals.

**(Choice E)** Trophozoites and cysts are seen in the stool of patients with intestinal protozoal infections such



1



Feedback



Suspend



End Block



Exhibit Display

*Strongyloides stercoralis*



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Zoom In

Zoom Out

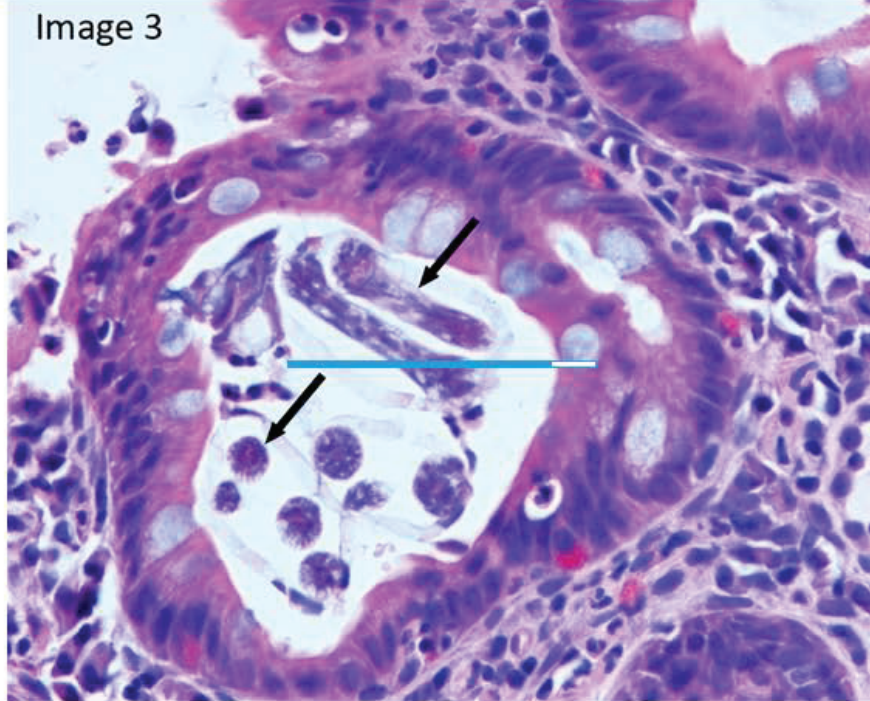
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My Notebook

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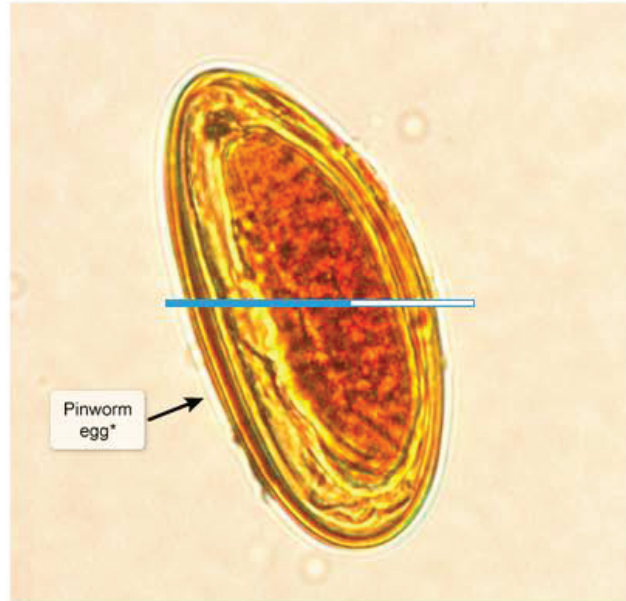
Image 3



Zoom In Zoom Out Reset New Existing My Notebook

Exhibit Display

*Enterobius vermicularis*



\*Identified with tape test

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Zoom In

Zoom Out

Reset

New | Existing

My Notebook





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

surrounding perianal folds. **Pinworm eggs** are best detected by examining a piece of scotch tape applied to the perianal region shortly after awakening.

**(Choice C)** Intestinal tapeworms (eg, *Taenia solium*, *T saginata*, *Diphyllobothrium latum*) are flatworms made up of multiple segments called proglottids. These are shed from the distal end of the worm and can be detected in the stool of infected individuals.

**(Choice E)** Trophozoites and cysts are seen in the stool of patients with intestinal protozoal infections such as *Giardia lamblia* and *Entamoeba histolytica*.

### Educational objective:

***Strongyloides stercoralis*** infection begins following **skin penetration** by filariform (infectious) larva and can be diagnosed by finding rhabditiform (noninfectious) **larvae in the stool**. Rhabditiform larvae can mature into filariform larva in the human gastrointestinal tract, precipitating an autoinfection cycle that occurs entirely within the affected individual. This can result in a **hyperinfection syndrome** characterized by massive dissemination of the organism, leading to multiorgan dysfunction and septic shock.

### References

- ***Strongyloides stercoralis* in the immunocompromised population.**



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

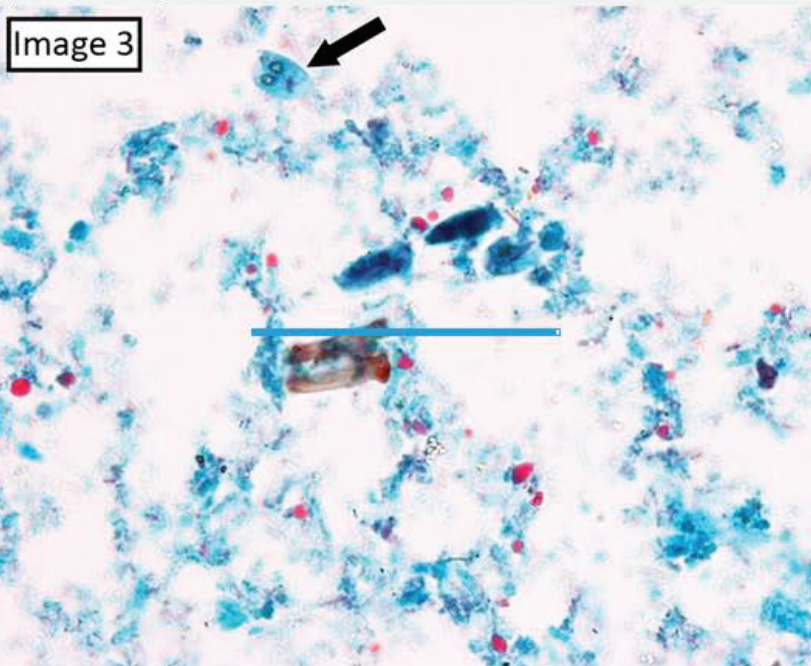
Calculator

Reverse Color

Text Zoom

Settings

## Exhibit Display

Giardia trophozoite and cysts Giardia trophozoite and cysts

Zoom In

Zoom Out

Reset

New | Existing

My Notebook





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

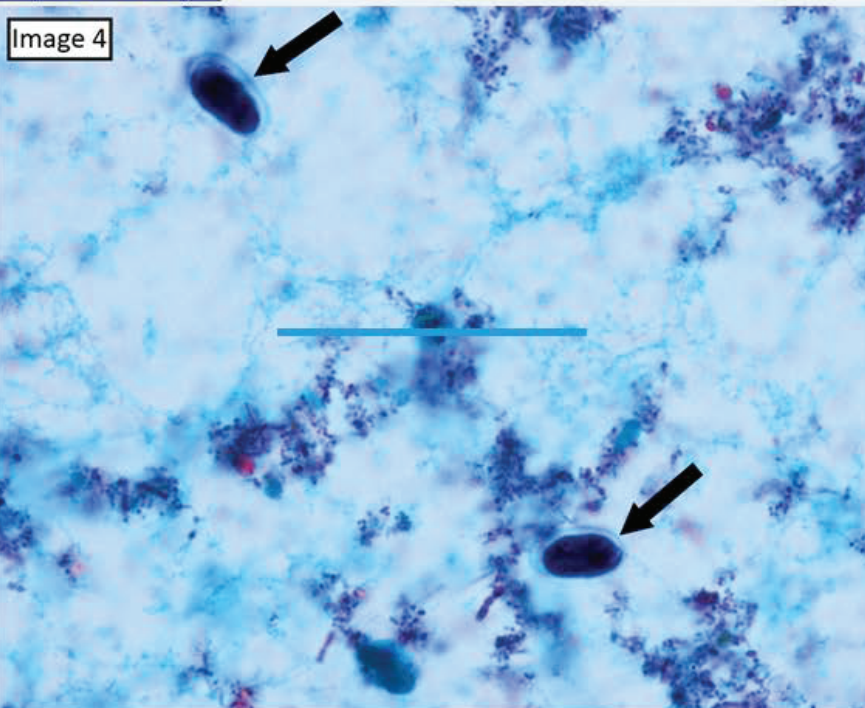
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Reverse Color

Text Zoom

Settings

## Exhibit Display

Giardia trophozoite and cysts [Giardia trophozoite and cysts](#)

Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block time remaining: 00:29:07

TUTOR

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End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



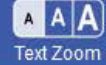
Notes



Calculator



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Text Zoom

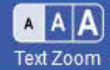
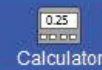
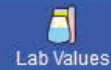


Settings

A 35-year-old alcoholic male is brought to the ER with hematemesis. Prior to this, he has had three episodes of vomiting. His BP is 110/80 mmHg and pulse is 98/min. He has no jaundice. Lungs are clear to auscultation. Abdomen is soft, non tender, and non-distended. There is no hepatomegaly. Endoscopy shows longitudinal mucosal tears at the gastroesophageal junction. This patient's condition is most likely related to which of the following?

- ☐ A. Intraabdominal pressure
- ☐ B. Venous pressure
- ☐ C. Local inflammation
- ☐ D. Acid reflux
- ☐ E. Mucosal ischemia

**Submit**

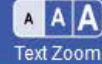
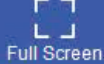


A 35-year-old alcoholic male is brought to the ER with **hematemesis**. Prior to this, he has had three episodes of vomiting. His BP is 110/80 mmHg and pulse is 98/min. He has no jaundice. Lungs are clear to auscultation. Abdomen is soft, non tender, and non-distended. There is no hepatomegaly. Endoscopy shows **longitudinal mucosal tears** at the gastroesophageal junction. This patient's condition is most likely related to which of the following?

- ✓ ☒ A. Intraabdominal pressure (60%)
- ☐ B. Venous pressure (11%)
- ☐ C. Local inflammation (4%)
- ☐ D. Acid reflux (19%)
- ☐ E. Mucosal ischemia (3%)

Correct

 60%  
Answered correctly 39 secs  
Time Spent 01/30/2021  
Last Updated



Longitudinal mucosal tears at the esophagogastric-squamocolumnar junction describe Mallory-Weiss syndrome. Most commonly, these tears occur secondary to rapid increase of intraabdominal and intraluminal gastric pressure, as when happens during retching and vomiting. Other precipitating factors include coughing, hiccupping, other repeated abdominal straining, and abdominal trauma. Additionally, hiatal hernias are found in about half of patients with Mallory-Weiss syndrome and are considered a strong predisposing factor. Mallory-Weiss syndrome is very commonly associated with alcoholism.

Mallory-Weiss tears can be asymptomatic or can lead to gastrointestinal hemorrhage that manifests as hematemesis. About 10% of all upper gastrointestinal bleeds are from Mallory-Weiss syndrome. The intensity of hemorrhage and amount of blood loss varies widely according to the length and depth of the tears, but is almost never life-threatening.

**(Choice B)** Increased venous pressure is associated with potentially life-threatening hemorrhage from esophageal varices. Esophageal varices occur in patients with cirrhosis who often have other symptoms of chronic liver disease—such as jaundice, spider nevi, palmar erythema, gynecomastia, and a history of alcohol abuse. Endoscopy is diagnostic.

**(Choices C and D)** Local inflammation plays a role in the development of chronic gastritis and







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

esophageal varices. Esophageal varices occur in patients with cirrhosis who often have other symptoms of chronic liver disease—such as jaundice, spider nevi, palmar erythema, gynecomastia, and a history of alcohol abuse. Endoscopy is diagnostic.

**(Choices C and D)** Local inflammation plays a role in the development of chronic gastritis and esophagitis. Acid reflux is characteristic of gastrointestinal reflux disease (GERD). Neither condition is known for significant upper GI bleeding.

**(Choice E)** Diminished blood perfusion to the small bowel and colon may result from arterial occlusion by embolus, thrombosis of the venous system, or low cardiac output. Ischemic bowel is the result, and it is a very dangerous condition. Ischemic bowel occurs most often in older patients.

### Educational Objective:

Mallory-Weiss tears account for about 10% of cases of upper GI hemorrhage. They occur due to increased intraluminal gastric pressure due to retching, vomiting, or other abdominal straining.

Pathology

Gastrointestinal &amp; Nutrition

Mallory-weiss syndrome

Subject

System

Topic

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 58-year-old woman comes to the office due to a week of pain with swallowing. Her symptoms have progressively worsened, and now she cannot eat comfortably. The patient has a history of hypertension, osteoporosis, and primary biliary cholangitis progressing to cirrhosis. She underwent a liver transplant 2 years ago and is on immunosuppressive therapy. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. The oropharynx is normal in appearance. Cardiopulmonary examination is unremarkable. The patient has epigastric tenderness with no abdominal distension or guarding. Upper endoscopy shows several small esophageal ulcerations with distinct borders located in the middle and lower portions of the esophagus. A biopsy taken at the edge of an ulcer shows giant cells and intranuclear eosinophilic inclusions. Which of the following is the most appropriate treatment for this patient?

- ☐ A. Acyclovir
- ☐ B. Alendronate
- ☐ C. Azithromycin
- ☒ D. Fluconazole
- ☐ E. Misoprostol



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

years ago and is on immunosuppressive therapy. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. The oropharynx is normal in appearance. Cardiopulmonary examination is unremarkable. The patient has epigastric tenderness with no abdominal distension or guarding. Upper endoscopy shows several small esophageal ulcerations with distinct borders located in the middle and lower portions of the esophagus. A biopsy taken at the edge of an ulcer shows giant cells and intranuclear eosinophilic inclusions. Which of the following is the most appropriate treatment for this patient?

- ☐ A. Acyclovir
- ☐ B. Alendronate
- ☐ C. Azithromycin
- ☐ D. Fluconazole
- ☐ E. Misoprostol
- ☐ F. Omeprazole
- ☐ G. Tenofovir

Submit

Block Time Remaining: 00:30:21

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Feedback

Suspend

End Block





years ago and is on immunosuppressive therapy. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. The oropharynx is normal in appearance. Cardiopulmonary examination is unremarkable. The patient has epigastric tenderness with no abdominal distension or guarding. Upper endoscopy shows several small esophageal ulcerations with distinct borders located in the middle and lower portions of the esophagus. A biopsy taken at the edge of an ulcer shows giant cells and intranuclear eosinophilic inclusions. Which of the following is the most appropriate treatment for this patient?

- ☒ A. Acyclovir (77%)
- ☐ B. Alendronate (0%)
- ☐ C. Azithromycin (2%)
- ☐ D. Fluconazole (4%)
- ☐ E. Misoprostol (1%)
- ☐ F. Omeprazole (8%)
- ☐ G. Tenofovir (5%)





## Explanation

**Esophagitis in an immunocompromised patient**

Pathogen	Endoscopic findings	Microscopic findings	Treatment
<b><i>Candida albicans</i></b>	Patches of adherent, grey/white pseudomembranes on erythematous mucosa	Yeast cells & pseudohyphae invading mucosal cells	Fluconazole
<b>HSV</b>	Small vesicles → "punched-out" ulcers	Eosinophilic intranuclear inclusions (Cowdry type A) in multinuclear squamous cells at ulcer margins	Acyclovir
<b>CMV</b>	Large, linear ulcerations	Intranuclear & cytoplasmic inclusions	Ganciclovir

**CMV** = cytomegalovirus; **HSV** = herpes simplex virus.

**Esophagitis** is usually the result of a noninfectious process such as gastroesophageal reflux disease.





**Esophagitis** is usually the result of a noninfectious process such as gastroesophageal reflux disease.

However, patients with **impaired cell-mediated immunity** (eg, chemotherapy, post-transplantation, AIDS) are also at risk for esophageal infections. The leading causes are *Candida*, cytomegalovirus, and **herpes simplex virus** (HSV).

HSV esophagitis usually presents with significant pain and discomfort with swallowing. Endoscopy typically reveals small vesicles or **punched-out ulcers** (ie, distinct borders) on the esophageal mucosa. Classic HSV findings on biopsy include **multinucleated giant cells** and **eosinophilic intranuclear inclusion bodies** (Cowdry type A). Treatment with oral **acyclovir** usually resolves the active infection, but latent virus can reactivate in the future, leading to recurrent symptoms.

**(Choice B)** Alendronate is a bisphosphonate used in the treatment of osteoporosis. Bisphosphonates can cause medication-induced esophagitis and could worsen this patient's symptoms.

**(Choice C)** Azithromycin can be used as part of the treatment for disseminated mycobacterium avium complex, which often involves the gastrointestinal tract. However, this condition usually occurs in those with advanced AIDS; the esophagus is affected less commonly than the intestine; and endoscopy typically reveals whitish-yellow nodules on the mucosa.

**(Choice D)** Fluconazole is used for candidal esophagitis. Endoscopy would reveal white







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

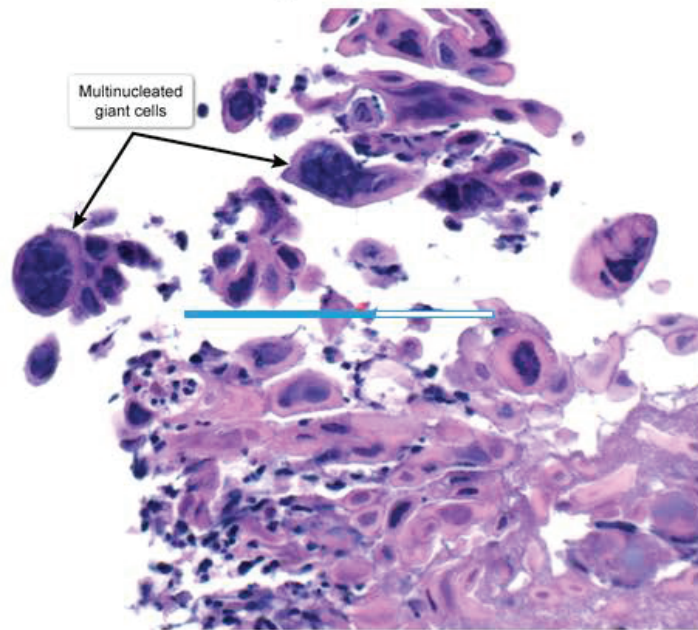
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**Esophagitis** is usually the result of a noninfectious process such as gastroesophageal reflux disease.

## Exhibit Display

## Herpes esophagitis



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1



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End Block



reveals whitish-yellow nodules on the mucosa.

**(Choice D)** Fluconazole is used for candidal esophagitis. Endoscopy would reveal white pseudomembranes on the esophageal mucosa, and histopathology would show yeasts with pseudohyphae.

**(Choice E)** Misoprostol is a prostaglandin analogue that significantly reduces gastric acid secretion and is sometimes used to prevent ulcers due to nonsteroidal antiinflammatory medication.

**(Choice F)** Proton pump inhibitors (eg, omeprazole) are used to treat erosive esophagitis from chronic reflux. Erosive esophagitis typically causes irregular ulcers along the esophageal mucosa, and biopsy would demonstrate inflammatory exudates and fibrinoid necrosis.

**(Choice G)** Tenofovir is an antiviral agent that can be used for HIV and chronic hepatitis B infections. Although tenofovir is an antiviral medication, it is not effective against HSV.

### Educational objective:

Herpes simplex virus esophagitis is most common in those with impaired cell-mediated immunity.

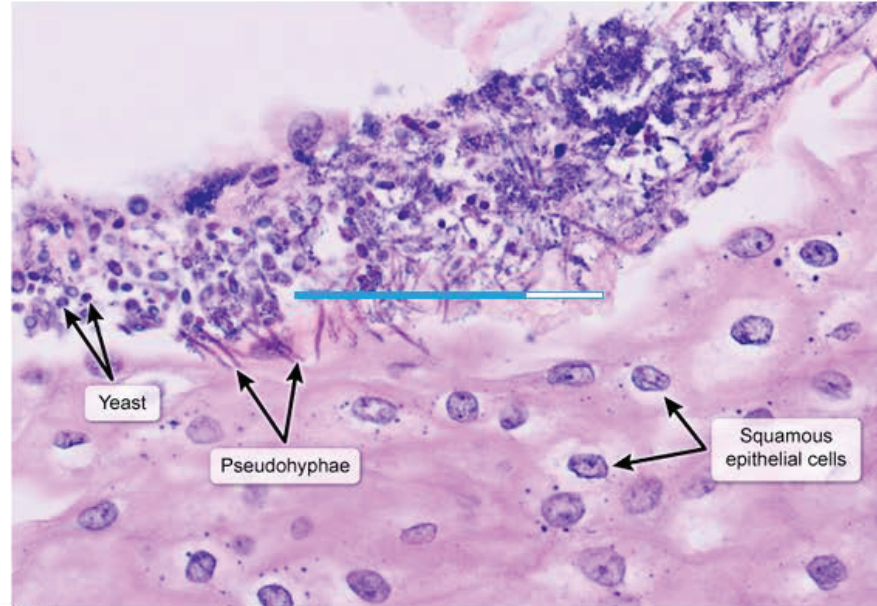
Endoscopy typically reveals small vesicles and "punched-out" ulcers. Findings on biopsy usually include multinucleated giant cells and eosinophilic intranuclear inclusions (Cowdry type A inclusion bodies).

Acyclovir is the treatment of choice.



### Exhibit Display

#### Candidal esophagitis



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Zoom Out

Reset

New | Existing

My Notebook





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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(Choice G) Tenofovir is an antiviral agent that can be used for HIV and chronic hepatitis B infections. Although tenofovir is an antiviral medication, it is not effective against HSV.

### Educational objective:

Herpes simplex virus esophagitis is most common in those with impaired cell-mediated immunity. Endoscopy typically reveals small vesicles and "punched-out" ulcers. Findings on biopsy usually include multinucleated giant cells and eosinophilic intranuclear inclusions (Cowdry type A inclusion bodies). Acyclovir is the treatment of choice.

Pathology

Gastrointestinal &amp; Nutrition

Esophagitis

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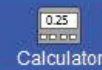
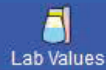
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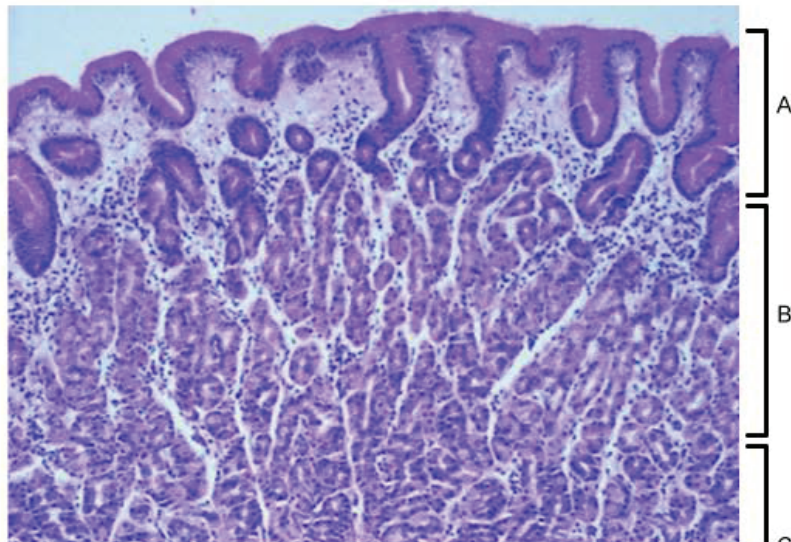
Suspend



End Block



A 65-year-old woman comes to the emergency department with progressive fatigue and lower-extremity paresthesias. Medical history is otherwise insignificant and the patient takes no medications. Laboratory studies show a mean corpuscular volume of 112 fL. Upper gastrointestinal endoscopy shows atrophic mucosa in the gastric body and fundus and a normal-appearing antrum. Destruction of which of the following gastric layers is most likely responsible for this patient's symptoms?



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16

17

18

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27

Item 1 of 40

Question Id: 124

Mark

Previous

Next

Full Screen

Tutorial

Lab Values

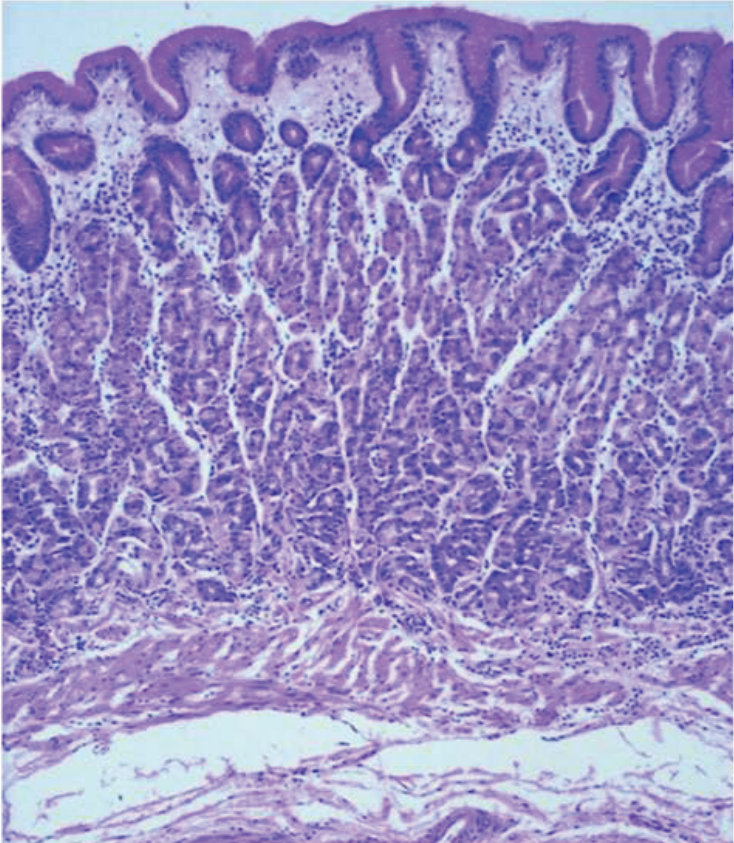
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Calculator

Reverse Color

Text Zoom

Settings



A

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Block Time Remaining: 00:00:06

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1

Feedback

Suspend

End Block



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16

17

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Item 1 of 40

Question Id: 124

Mark

Previous

Next

Full Screen

Tutorial

Lab Values

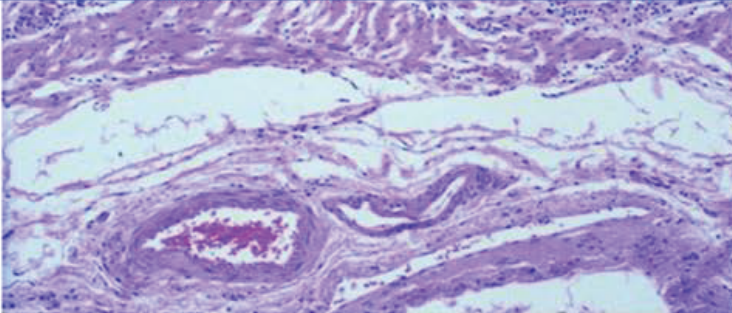
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☐ A.A

☐ B.B

☐ C.C

☐ D.D

☐ E.E

Submit

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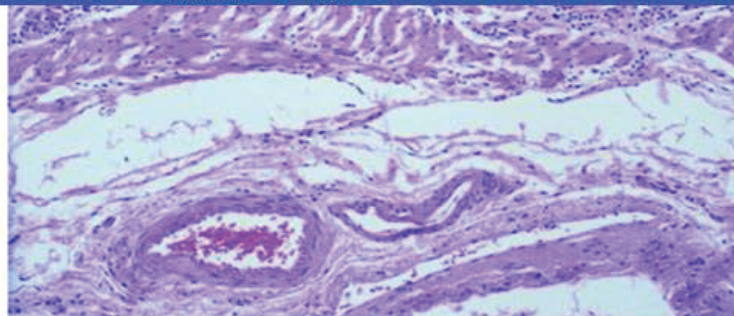
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- ☐ A.A (30%)
- ☒ B.B (52%)
- ☐ C.C (13%)
- ☐ D.D (1%)
- ☐ E.E (1%)

Correct



52%

Answered correctly



12 secs

Time spent



11/11/2020

Last updated

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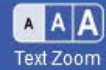
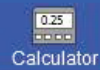
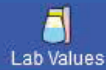
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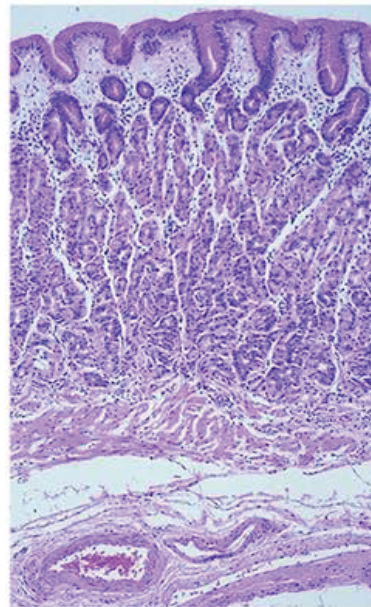


End Block



### Exhibit Display

#### Normal gastric histology



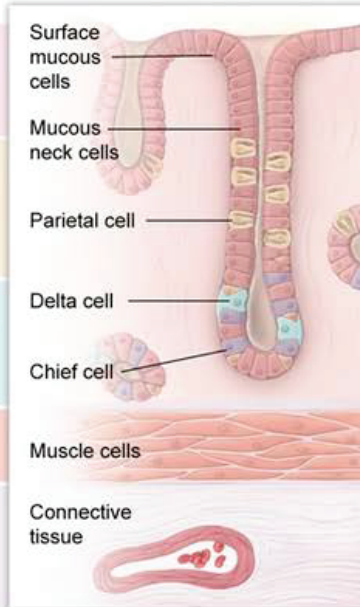
Simple columnar epithelial cells

Upper glandular layer

Deeper aspect of gastric glands

Muscularis mucosae

Submucosa



Surface mucous cells

Mucous neck cells

Parietal cell

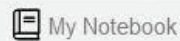
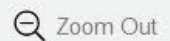
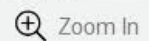
Delta cell

Chief cell

Muscle cells

Connective tissue

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The combination of lower-extremity paresthesias, macrocytic red blood cells (RBCs), and gastric body and fundal atrophy is highly suggestive of **pernicious anemia (PA)**. PA is an autoimmune disorder caused by the cell-mediated **destruction of parietal cells**, oxyntic (pale pink) cells found predominantly in the **upper glandular layer** of the gastric body and fundus. Over time, progressive parietal cell destruction leads to chronic atrophic gastritis (ie, autoimmune gastritis), characterized histologically by a CD4-predominate inflammatory infiltrate, **oxyntic gland** atrophy, and intestinal metaplasia (ie, replacement of normal epithelia with goblet cells).

Parietal cells are responsible for the secretion of hydrochloric acid and intrinsic factor, a glycoprotein that is involved in the absorption of  $B_{12}$  (cobalamin, an essential nutrient). After a critical number of parietal cells are destroyed and hepatic stores of cobalamin are depleted, patients **develop  $B_{12}$  deficiency**. This results in a **megaloblastic anemia**, characterized by macro-ovalocytes (elevated mean corpuscular volume, oval-shaped RBCs) and hypersegmented neutrophils. Patients also develop neurologic dysfunction due to demyelination of the dorsal and lateral spinal tracts, resulting in **paresthesias and ataxia**.

**(Choice A)** This region contains simple columnar epithelial cells that secrete mucus to protect the gastric lining from acid.





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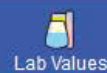
Next



Full Screen



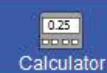
Tutorial



Lab Values



Notes



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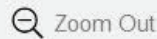
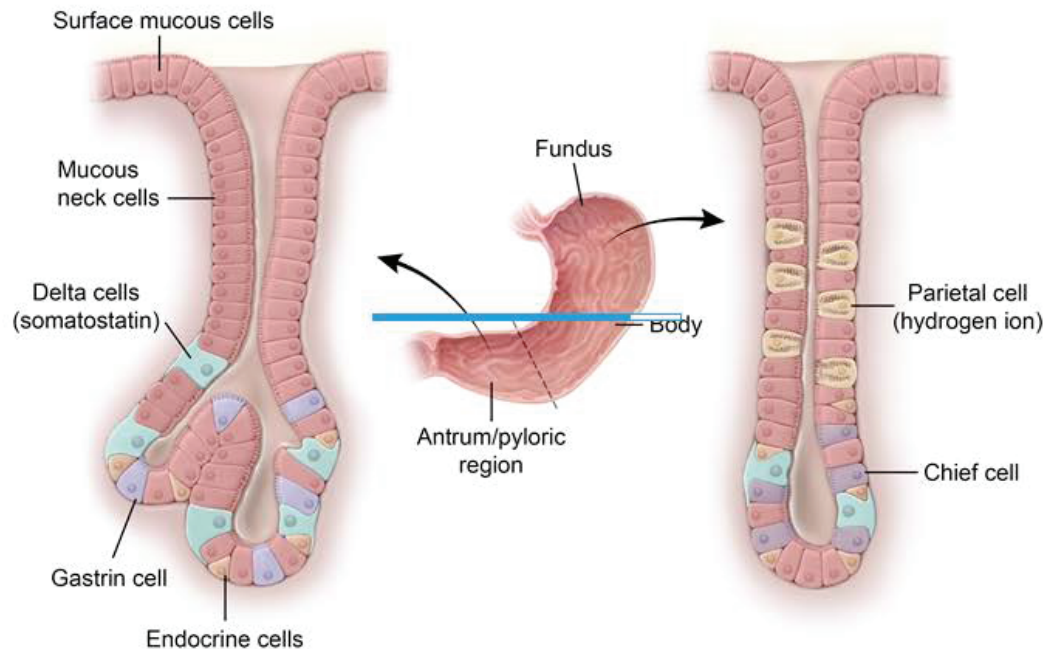


Settings

Exhibit Display

Pyloric gland

Oxyntic gland



Existing



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**(Choice A)** This region contains simple columnar epithelial cells that secrete mucus to protect the gastric lining from acid.

**(Choice C)** In contrast to the parietal cell-rich superficial gastric glands, the deeper region of the gastric glands has a preponderance of small, basophilic, granular chief cells that synthesize and secrete pepsinogen. Pyloric glands contain enteroendocrine cells with apical nuclei and light cytoplasm that produce gastrin and somatostatin.

**(Choice D)** This region contains the muscularis mucosae, which separates the lamina propria from the submucosa.

**(Choice E)** This region contains the submucosa, which consists of well-vascularized connective tissue.

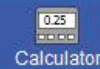
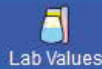
**Educational objective:**

Pernicious anemia is an autoimmune disorder caused by the cell-mediated destruction of parietal cells in the superficial upper glandular layer of the gastric body and fundus. Parietal cells are responsible for the secretion of hydrochloric acid and intrinsic factor, a glycoprotein involved in the absorption of B<sub>12</sub>.

Deficiency leads to megaloblastic anemia and neurologic dysfunction.







A 72-year-old man comes to the office due to constipation. His stools have become increasingly hard, small-volume, and difficult to pass. This has been associated with bloating but not vomiting. Symptoms have not improved despite fiber supplementation, polyethylene glycol, and bisacodyl. The patient was recently diagnosed with metastatic pancreatic cancer and was prescribed palliative chemotherapy 2 months ago. His cancer causes severe abdominal pain, which requires high-dose oxycodone to control. Vital signs are within normal limits. The abdomen is mildly distended with decreased bowel sounds. Which of the following medications acts as a  $\mu$ -opioid receptor antagonist that could alleviate this patient's constipation without inducing withdrawal symptoms?

- ☐ A. Diphenoxylate
- ☐ B. Loperamide
- ☐ C. Lubiprostone
- ☐ D. Methylnaltrexone
- ☐ E. Naloxone





small-volume, and difficult to pass. This has been associated with bloating but not vomiting. Symptoms have not improved despite fiber supplementation, polyethylene glycol, and bisacodyl. The patient was recently diagnosed with metastatic pancreatic cancer and was prescribed palliative chemotherapy 2 months ago. His cancer causes severe abdominal pain, which requires high-dose oxycodone to control. Vital signs are within normal limits. The abdomen is mildly distended with decreased bowel sounds. Which of the following medications acts as a  $\mu$ -opioid receptor antagonist that could alleviate this patient's constipation without inducing withdrawal symptoms?

- ☐ A. Diphenoxylate (10%)
- ☐ B. Loperamide (32%)
- ☐ C. Lubiprostone (7%)
- ☒ D. Methylnaltrexone (40%)
- ☐ E. Naloxone (8%)

Correct

40%



54 secs



02/16/2021

Block Time Remaining: 00:01:06

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1



Feedback



Suspend



End Block



### Anticonstipation agents

**Bulk-forming laxatives**

(eg, fiber supplements)

- Binds luminal water to decrease consistency of stool
- Side effects: flatulence, abdominal distension

**Osmotic laxatives**

(eg, polyethylene glycol, magnesium hydroxide, lactulose)

- Osmotically active agent that draws water into the lumen
- Side effects: electrolyte disturbances, bloating

**Surfactant**

(eg, docusate)

- Decreases stool surface tension, enabling water to enter stool
- Side effects: rare

**Stimulant laxatives**

(eg, bisacodyl, senna)

- Activates enteric nerves in myenteric plexus to stimulate peristalsis
- Side effects: abdominal cramping, electrolyte disturbances

**Chloride channel agonist**

- Causes chloride efflux into intestinal lumen, which is followed by sodium and water





(eg, polyethylene glycol, magnesium hydroxide, lactulose)	<ul style="list-style-type: none"> <li>• Side effects: electrolyte disturbances, bloating</li> </ul>
<b>Surfactant</b> (eg, docusate)	<ul style="list-style-type: none"> <li>• Decreases stool surface tension, enabling water to enter stool</li> <li>• Side effects: rare</li> </ul>
<b>Stimulant laxatives</b> (eg, bisacodyl, senna)	<ul style="list-style-type: none"> <li>• Activates enteric nerves in myenteric plexus to stimulate peristalsis</li> <li>• Side effects: abdominal cramping, electrolyte disturbances</li> </ul>
<b>Chloride channel agonist</b> (eg, lubiprostone)	<ul style="list-style-type: none"> <li>• Causes chloride efflux into intestinal lumen, which is followed by sodium and water</li> <li>• Side effects: headache, nausea</li> </ul>
<b>Peripherally acting <math>\mu</math>-opioid receptor antagonists</b> (eg, methylnaltrexone)	<ul style="list-style-type: none"> <li>• Counteracts inhibitory effect of opioids on peristalsis</li> <li>• Side effects: rare (does not cause opiate withdrawal)</li> </ul>

\*All constipation medications can cause diarrhea at high doses.



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

All constipation medications can cause diarrhea at high doses.

This patient has **opioid-induced constipation** (OIC). Opiates (eg, oxycodone) exert their analgesic effects by binding to opiate receptors in the central and peripheral nervous systems, reducing nociceptive transmission and the perception of pain. Constipation, the most common side effect of opiate therapy, occurs due to the activation of  **$\mu$ -opiate receptors** in the gastrointestinal tract. This results in decreased intestinal peristaltic activity and inhibition of ion and fluid secretion, leading to desiccated, pellet-like stool. Unlike many other opiate side effects, tolerance to constipation does not readily occur. Therefore, all patients on opiate therapy should be considered for prophylactic laxative therapy (eg, docusate, polyethylene glycol, bisacodyl).

Those with refractory OIC may benefit from **methylnaltrexone**, a peripherally acting  **$\mu$ -opioid receptor antagonist** that reverses the anti-peristaltic effect of opiates. It does not cross the blood-brain barrier; therefore, it **does not induce** opiate-related **withdrawal symptoms**, allowing for treatment of OIC without disrupting analgesic effects.

**(Choices A and B)** Diphenoxylate and loperamide are both opiate-based medications designed to inhibit peristalsis in the gastrointestinal tract. These medications are used to treat diarrhea and would worsen this patient's constipation.



1



Feedback



Suspend



End Block



disrupting analgesic effects.

**(Choices A and B)** Diphenoxylate and loperamide are both opiate-based medications designed to inhibit peristalsis in the gastrointestinal tract. These medications are used to treat diarrhea and would worsen this patient's constipation.

**(Choice C)** Lubiprostone is a chloride channel agonist that increases intestinal secretions. Although it is not a  $\mu$ -opioid receptor antagonist, it can be used to treat OIC and would not put patients at risk for opiate-related withdrawal.

**(Choice E)** Naloxone is also an opioid receptor antagonist; however, unlike methylnaltrexone, naloxone crosses the blood-brain barrier. It induces symptoms of withdrawal and reversal of analgesia and is used to treat acute opioid toxicity (eg, respiratory depression, somnolence).

### Educational objective:

Constipation is the most common side effect of opiate therapy and occurs due to the binding of  $\mu$ -opioid receptors in the gastrointestinal tract, which decreases intestinal motility and inhibits ion and fluid secretion. Methylnaltrexone, a peripherally acting  $\mu$ -opioid receptor antagonist that does not cross the blood-brain barrier, can alleviate opioid-induced constipation without inducing opiate-related withdrawal symptoms.







A 32-year-old female presents to your office with severe nausea and recurrent bilious vomiting. Her symptoms initially began as postprandial epigastric pain and early satiety, but have progressed over the last two weeks. She works as an actress, and tells you that her symptoms only started when she "landed a role in a soap opera" and was inspired to lose 25 lbs. on a "crash diet". On physical exam, her abdomen is tender and slightly distended with high-pitched bowel sounds. Concerned about a small bowel obstruction, you admit the patient to the hospital. A laparotomy is performed, and it is observed that the angle between her superior mesenteric artery and her aorta is significantly decreased. Which of the following structures is most likely to be obstructed by the artery?

- ☐ A. Ascending portion of the duodenum
- ☐ B. Descending portion of the duodenum
- ☐ C. Duodenal bulb
- ☐ D. Duodenojejunal flexure
- ☐ E. Gastric antrum
- ☐ F. Transverse portion of the duodenum





last two weeks. She works as an actress, and tells you that her symptoms only started when she "landed a role in a soap opera" and was inspired to lose 25 lbs. on a "crash diet". On physical exam, her abdomen is tender and slightly distended with high-pitched bowel sounds. Concerned about a small bowel obstruction, you admit the patient to the hospital. A laparotomy is performed, and it is observed that the angle between her superior mesenteric artery and her aorta is significantly decreased. Which of the following structures is most likely to be obstructed by the artery?

- ☐ A. Ascending portion of the duodenum (4%)
- ☐ B. Descending portion of the duodenum (9%)
- ☐ C. Duodenal bulb (5%)
- ☐ D. Duodenojejunal flexure (15%)
- ☐ E. Gastric antrum (2%)
- ☒ F. Transverse portion of the duodenum (62%)

Correct

62%



54 secs



12/21/2020

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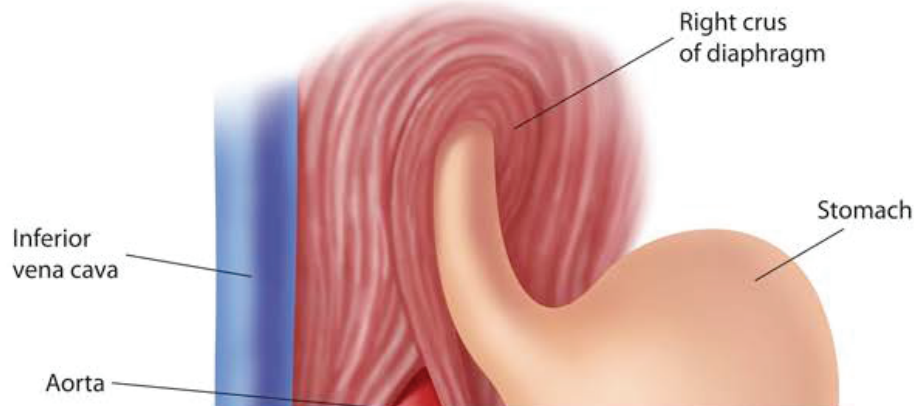
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The superior mesenteric artery (SMA) leaves the aorta at the level of L1 and supplies the intestine from the duodenum and pancreas to the left colic flexure. The transverse portion of the duodenum lies horizontally at the level of L3, between the aorta and superior mesenteric artery. Normally, the SMA and aorta form an approximately 45 degree angle. If this angle diminishes to less than 20 degrees, the transverse portion of the duodenum can get entrapped between the SMA and aorta, leading to symptoms of partial small bowel obstruction. This condition is called superior mesenteric artery syndrome.

Superior mesenteric artery syndrome  
Anterior view







Item 3 of 40

Question Id: 303



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

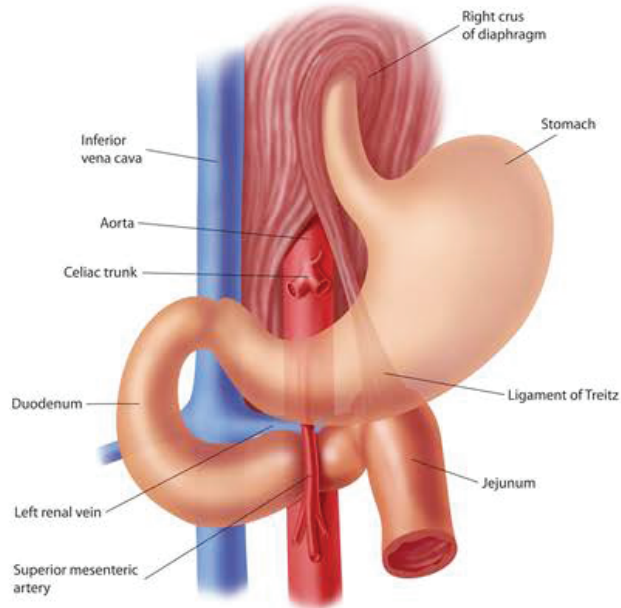
Calculator

Reverse Color

Text Zoom

Settings

## Exhibit Display

Superior mesenteric artery syndrome  
Anterior view

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Superior mesenteric artery

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Narrowing of the aortomesenteric angle can occur with any condition that causes **diminished mesenteric fat**, including low body weight, recent weight loss, severe burns or other inducers of catabolism, and prolonged bed rest. It can also occur with pronounced lordosis or after surgical correction of scoliosis, as this procedure lengthens the spine resulting in decreased mobility of the SMA.

### Educational Objective:

Superior mesenteric artery syndrome occurs when the transverse portion of the duodenum is entrapped between the SMA and aorta, causing symptoms of partial intestinal obstruction. This syndrome occurs when the aortomesenteric angle critically decreases, secondary to diminished mesenteric fat, pronounced lordosis, or surgical correction of scoliosis.

Anatomy

Gastrointestinal & Nutrition

Bowel obstruction

Subject

System

Topic

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Previous

Next



Full Screen



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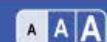
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Calculator



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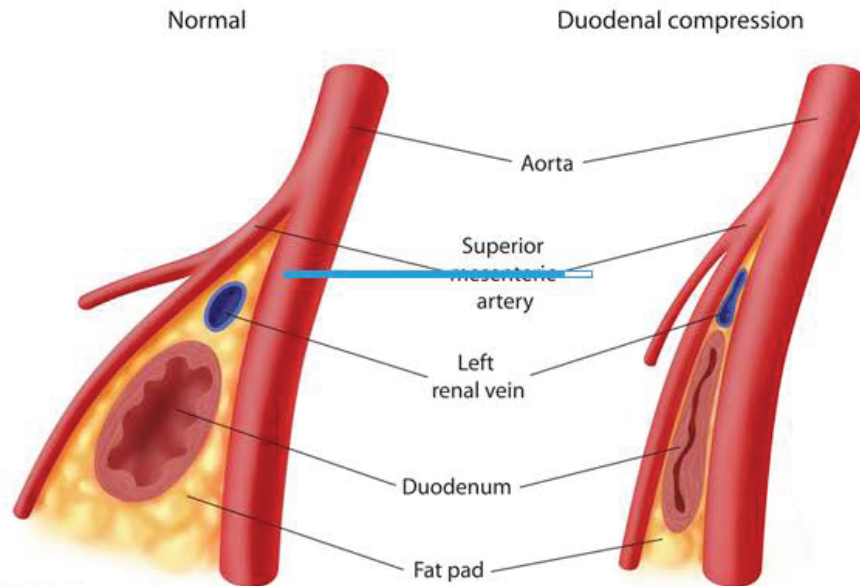


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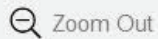
## Exhibit Display

Superior mesenteric artery syndrome  
Lateral view

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End Block





A 3-year-old boy is brought to the physician's office by his parents because of abdominal pain. Physical examination reveals rectal bleeding, and the patient undergoes an appropriate diagnostic workup. Laparotomy is then performed. Surgical findings include a blind pouch connected to the ileum, with a fibrous band seen attaching the end of the pouch to the umbilicus. The walls of this pouch are most likely composed of which of the following?

- ☐ A. Fibrous tissue
- ☐ B. Granulation tissue and peritoneum
- ☐ C. Mucosa and submucosa layers
- ☐ D. Omentum and adipose tissue
- ☐ E. Mucosa, submucosa, and muscular layers

Submit





A 3-year-old boy is brought to the physician's office by his parents because of abdominal pain. Physical examination reveals rectal bleeding, and the patient undergoes an appropriate diagnostic workup. Laparotomy is then performed. Surgical findings include a **blind pouch** connected to the ileum, with a fibrous band seen attaching the end of the pouch to the umbilicus. The walls of this pouch are most likely composed of which of the following?

- ☐ A. Fibrous tissue (3%)
- ☐ B. Granulation tissue and peritoneum (3%)
- ☐ C. Mucosa and submucosa layers (17%)
- ☐ D. Omentum and adipose tissue (2%)
- ☒ E. Mucosa, submucosa, and muscular layers (72%)

Correct



72%

Answered correctly



40 secs

Time Spent



12/21/2020

Last Updated

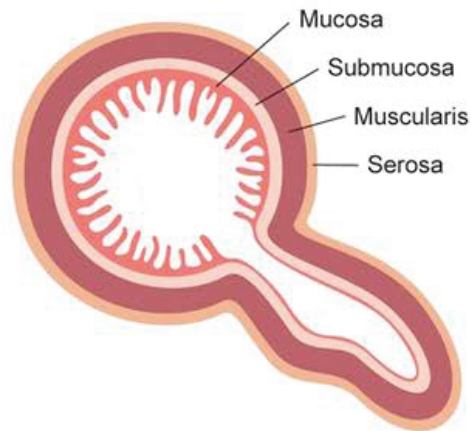




## Exhibit Display

## True &amp; false diverticula

## True diverticulum



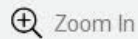
Examples:  
Meckel diverticula,  
normal appendix

## Pseudodiverticulum



Examples:  
Zenker esophageal diverticula,  
diverticulosis

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During early embryogenesis, the lumen of the midgut and yolk sac cavity are connected via the omphalomesenteric (vitelline) duct. This duct normally obliterates during the 7<sup>th</sup> week of fetal life. Partial failure of this duct to obliterate leads to the formation of Meckel's diverticulum. Meckel's diverticulum may present with rectal bleeding or intestinal obstruction; however, most cases are asymptomatic. Remember the rule of 2's with Meckel's diverticulum: 2% of the population, 2 feet from the ileocecal valve, 2 inches in length, 2% are symptomatic, and males are 2 times more likely to be affected.

In contrast to false diverticula, which contain mucosa and submucosa only, Meckel's diverticulum is a true diverticulum, consisting of all three parts of the intestinal wall: mucosa, submucosa, and muscularis. It also often contains ectopic mucosa-gastric epithelium being the most common (pancreatic tissue is the next most common). This ectopic gastric tissue secretes gastric acid that can cause ulceration of adjacent mucosa and lower GI bleeding (melena/hematochezia).

**(Choice C)** False diverticula contain only mucosa and submucosa. These layers herniate through defects in the muscular layer. Colonic and Zenker (upper esophageal) diverticula are examples of false (pulsion) diverticula.

**(Choices A, B, & D)** Fibrous tissue, granulation tissue, and omentum are not histologically present in Meckel's diverticulum. In addition to containing all three portions of the intestinal wall, Meckel's



most common). This ectopic gastric tissue secretes gastric acid that can cause ulceration of adjacent mucosa and lower GI bleeding (melena/hematochezia).

**(Choice C)** False diverticula contain only mucosa and submucosa. These layers herniate through defects in the muscular layer. Colonic and Zenker (upper esophageal) diverticula are examples of false (pulsion) diverticula.

**(Choices A, B,& D)** Fibrous tissue, granulation tissue, and omentum are not histologically present in Meckel's diverticulum. In addition to containing all three portions of the intestinal wall, Meckel's diverticulum may also contain ectopic tissue, such as gastric or pancreatic tissue.

### Educational objective:

Meckel's diverticulum is a remnant of the omphalomesenteric (vitelline) duct. It is connected to the ileum and is located 2 feet proximal to the ileocecal valve. It often contains acid-secreting ectopic gastric tissue, which may cause ulceration of the adjacent mucosa and lower GI bleeding (melena/hematochezia).

Meckel's diverticulum is a true diverticulum and consists of all parts of the intestinal wall.

### References

- [Meckel diverticulum: the Mayo Clinic experience with 1476 patients \(1950-2002\).](#)

Embryology      Gastrointestinal & Nutrition      Meckel diverticulum

Block Time Remaining: 00:02:40

TUTOR

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A 3-month-old boy is evaluated for large-volume diarrhea and failure to thrive. The patient was born via spontaneous vaginal delivery at 38 weeks gestation. His mother reports that the pregnancy was uncomplicated and there is no family history of gastrointestinal disease. Physical examination shows mild abdominal distension, muscle wasting, and pitting edema. Histochemical evaluation reveals absence of enteropeptidase activity in the proximal intestinal villi. Activity of which of the following substances is most likely impaired in this patient?

- ☐ A. Amylase
- ☐ B. Bile salts
- ☐ C. Lactase
- ☐ D. Pepsin
- ☐ E. Secretin
- ☐ F. Trypsin

**Submit**

Block Time Remaining: 00:02:42

TUTOR

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Feedback



Suspend



End Block





A 3-month-old boy is evaluated for large-volume diarrhea and failure to thrive. The patient was born via spontaneous vaginal delivery at 38 weeks gestation. His mother reports that the pregnancy was uncomplicated and there is no family history of gastrointestinal disease. Physical examination shows mild abdominal distension, muscle wasting, and pitting edema. Histochemical evaluation reveals absence of enteropeptidase activity in the proximal intestinal villi. Activity of which of the following substances is most likely impaired in this patient?

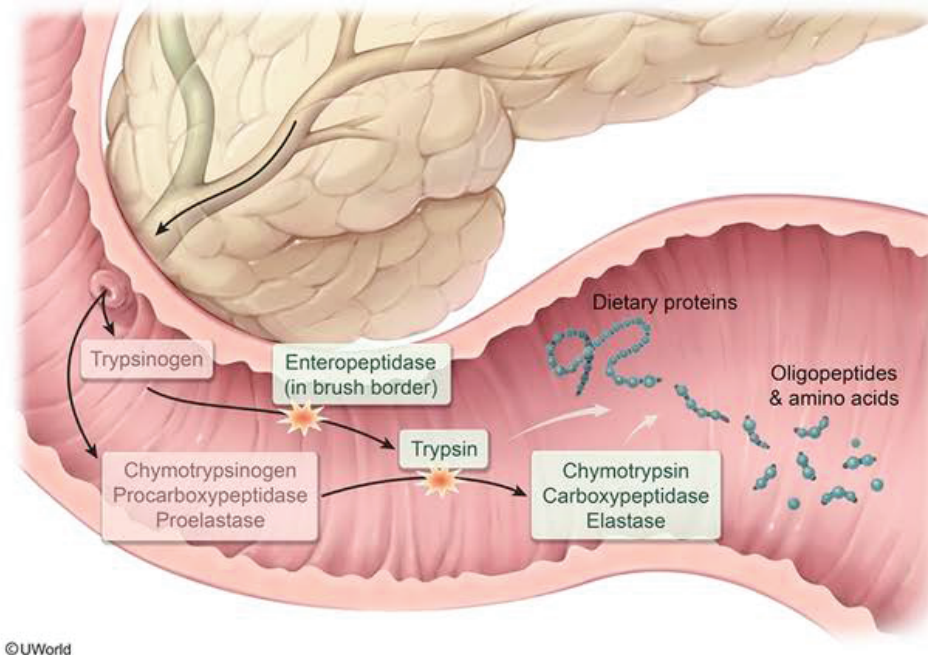
- ☐ A. Amylase (2%)
- ☐ B. Bile salts (1%)
- ☐ C. Lactase (13%)
- ☐ D. Pepsin (10%)
- ☐ E. Secretin (3%)
- ☒ F. Trypsin (69%)





## Exhibit Display

## Pancreatic enzyme activation



Zoom In

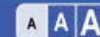
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Although chemical digestion of proteins begins in the stomach, the majority of enzymatic breakdown and absorption occurs in the small intestine. Dietary proteins exist predominately as polypeptides; in order to be absorbed, they must be hydrolyzed to tripeptides, dipeptides, and amino acids. Hydrolysis begins in the stomach with the activation of pepsin by hydrochloric acid; it continues in the proximal small intestine, catalyzed by the pancreatic enzymes trypsin, chymotrypsin, carboxypeptidase, and elastase.

Pancreatic enzymes, including trypsin, are secreted in their inactive forms. **Enteropeptidase**, a duodenal brush border enzyme, is responsible for **activation of trypsin** from its inactive precursor, trypsinogen. Once active, trypsin functions to cleave peptide bonds in dietary proteins and activate the other pancreatic enzymes. Enteropeptidase **deficiency** leads to both **protein and fat malabsorption** as trypsin is required to activate enzymes required for both lipid and protein digestion. The disease causes **diarrhea, failure to thrive, and edema** (due to hypoproteinemia).

**(Choice A)** Amylase is produced by the salivary glands and pancreas; it catalyzes the hydrolysis of complex carbohydrates to simple sugars.

**(Choice B)** Bile salts are formed through bile acid conjugation with amino acids glycine and taurine. This increases their solubility, allowing them to aid in lipid digestion and absorption through the formation of







**(Choice A)** Amylase is produced by the salivary glands and pancreas; it catalyzes the hydrolysis of complex carbohydrates to simple sugars.

**(Choice B)** Bile salts are formed through bile acid conjugation with amino acids glycine and taurine. This increases their solubility, allowing them to aid in lipid digestion and absorption through the formation of micelles.

**(Choice C)** Lactase is produced by the intestinal brush border and is responsible for the hydrolysis of lactose to glucose and galactose. Lactase non-persistence commonly develops during mid-childhood, resulting in lactose intolerance.

**(Choice D)** Chief cells of the stomach release the inactive form of pepsin, pepsinogen. Exposure to hydrochloric acid in the stomach activates pepsin, initiating protein digestion.

**(Choice E)** Secretin is a peptide hormone secreted by the S cells of the duodenum; it stimulates the secretion of bicarbonate from the pancreas and inhibits gastric acid secretion in the stomach. Neutralization of the acidic pH of food entering the duodenum from the stomach is necessary for the proper function of pancreatic enzymes.

**Educational objective:**





**(Choice C)** Lactase is produced by the intestinal brush border and is responsible for the hydrolysis of lactose to glucose and galactose. Lactase non-persistence commonly develops during mid-childhood, resulting in lactose intolerance.

**(Choice D)** Chief cells of the stomach release the inactive form of pepsin, pepsinogen. Exposure to hydrochloric acid in the stomach activates pepsin, initiating protein digestion.

**(Choice E)** Secretin is a peptide hormone secreted by the S cells of the duodenum; it stimulates the secretion of bicarbonate from the pancreas and inhibits gastric acid secretion in the stomach. Neutralization of the acidic pH of food entering the duodenum from the stomach is necessary for the proper function of pancreatic enzymes.

### Educational objective:

The duodenal brush border enzyme enteropeptidase activates trypsin from its inactive precursor, trypsinogen. Trypsin degrades complex polypeptides to dipeptides, tripeptides, and amino acids while activating other pancreatic enzymes. Enteropeptidase deficiency impairs both protein and fat absorption, leading to diarrhea, failure to thrive, and hypoproteinemia.

Physiology

Gastrointestinal &amp; Nutrition

Malabsorption

Subject

System

Topic

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Feedback



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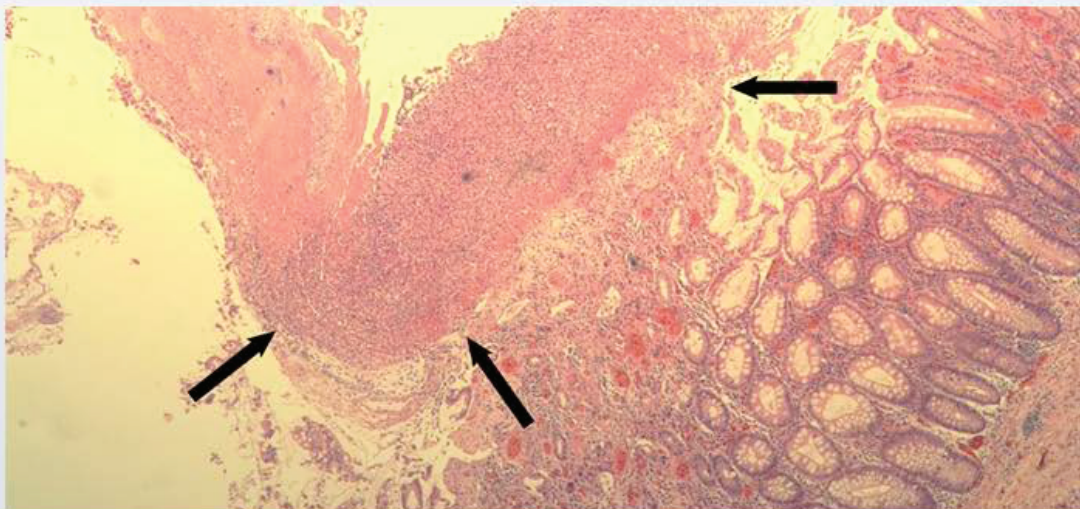


End Block





A 46-year-old HIV-positive man is hospitalized with fever, cramping abdominal pain, and watery diarrhea. Evaluation shows high fever, hypotension, tachycardia, and lower abdominal distension and tenderness. Abdominal x-ray reveals free intraperitoneal air, and the patient is taken for urgent exploratory laparotomy. Operative findings include an erythematous and dilated colon. A focus of bowel wall necrosis with perforation is resected. Histopathology reveals acute inflammatory changes and epithelial necrosis as shown below.







Item 6 of 40

Question Id: 6510



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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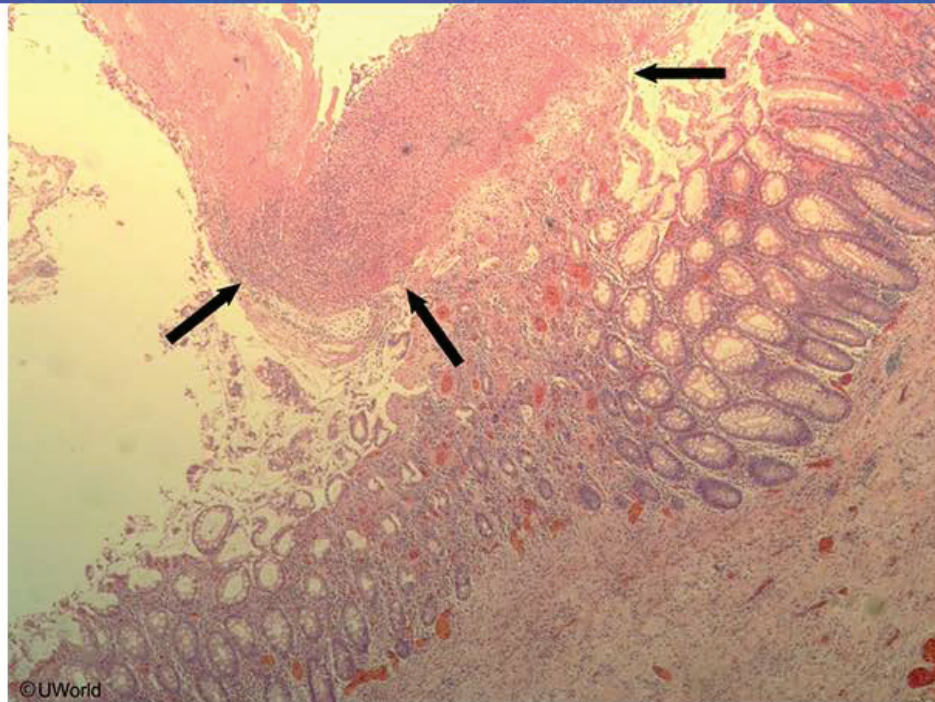


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### Exhibit Display



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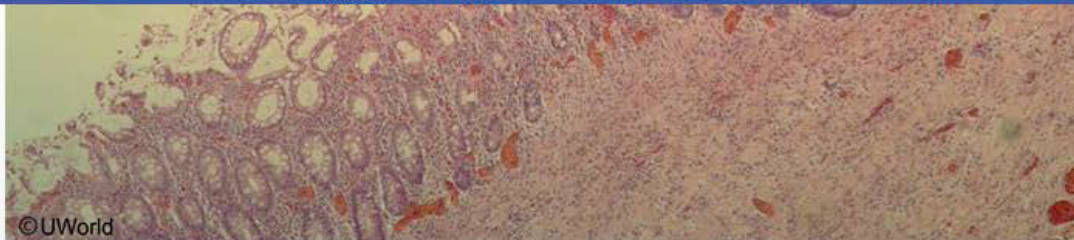
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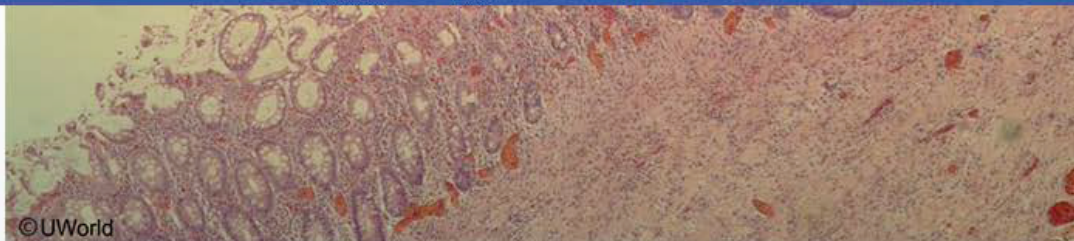


There is a layer of denuded epithelium, fibrin, and inflammatory cells overlaying the mucosa (see arrows). Which of the following is the most likely responsible pathogen?

- ☐ A. *Campylobacter jejuni*
- ☐ B. *Clostridium difficile*
- ☐ C. *Salmonella typhi*
- ☐ D. *Shigella flexneri*
- ☐ E. *Vibrio cholerae*

Submit





There is a layer of denuded epithelium, fibrin, and inflammatory cells overlaying the mucosa (see arrows). Which of the following is the most likely responsible pathogen?

- ☐ A. *Campylobacter jejuni* (6%)
- ☒ B. *Clostridium difficile* (64%)
- ☐ C. *Salmonella typhi* (11%)
- ☐ D. *Shigella flexneri* (9%)
- ☐ E. *Vibrio cholerae* (7%)

Correct

64%  
Answered correctly03 mins, 40 secs  
Time Spent02/11/2021  
Last Updated

Block Time Remaining: 00:06:53

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Feedback



Suspend



End Block





This patient with diarrhea, abdominal pain, and fever developed a colonic perforation. In conjunction with the pseudomembrane demonstrated on histology, this presentation is highly suggestive of ***Clostridium difficile* infection** (CDI). *C difficile* is an anaerobic, spore-forming, toxigenic, gram-positive rod that causes infectious colitis. The most significant risk factor for the development of CDI is antibiotic use. Antibiotics (particularly clindamycin, fluoroquinolones, and cephalosporins) alter the normal bowel flora, thereby predisposing to *C difficile* overgrowth. Other risk factors include hospitalization, older age, and proton pump inhibitor use.

*C difficile* produces 2 toxins: Toxin A (enterotoxin) and Toxin B (cytotoxin). These toxins disrupt cellular cytoskeletons and intercellular tight junctions, leading to colonocyte apoptosis. The colonic mucosa responds to toxin exposure by forming white, patchy **pseudomembranes**, which consist of a **neutrophil-predominant** inflammatory infiltrate, **fibrin**, bacteria, and necrotic epithelium. Patients with severe disease may develop a nonobstructive colonic dilation known as **toxic megacolon**, which leads to increased risk of colonic perforation (as seen in this patient).

**(Choice A)** *Campylobacter jejuni* is associated with watery diarrhea that may become bloody, abdominal cramping, and fever. Neutrophilic infiltrate and crypt abscesses are identified on histology.

**(Choice C)** *Salmonella typhi* causes typhoid fever, which manifests with bloody diarrhea, abdominal pain,





Item 6 of 40

Question Id: 6510



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



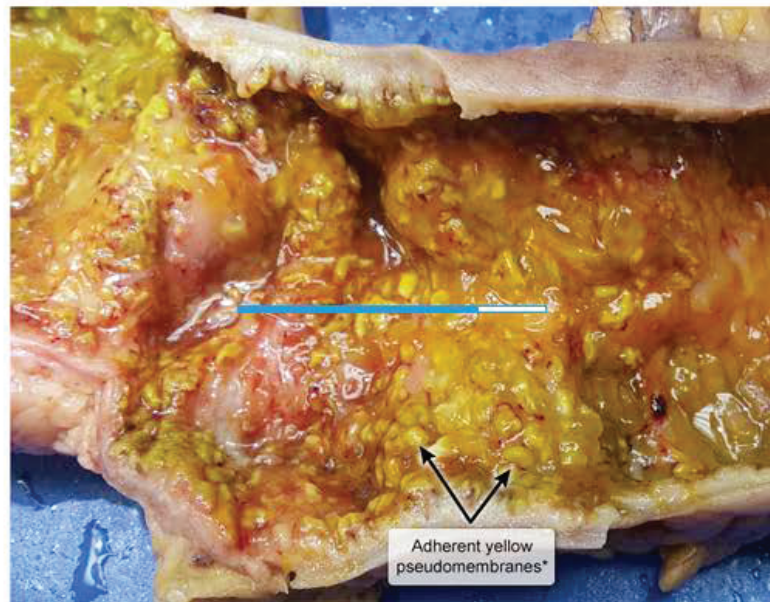
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## Exhibit Display

## Pseudomembranous colitis

Adherent yellow  
pseudomembranes\*\*Fibrin and inflammatory debris associated with *Clostridioides* (formerly *Clostridium*) *difficile*

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End Block



(Choice A) *Campylobacter jejuni* is associated with watery diarrhea that may become bloody, abdominal cramping, and fever. Neutrophilic infiltrate and crypt abscesses are identified on histology.

(Choice C) *Salmonella typhi* causes typhoid fever, which manifests with bloody diarrhea, abdominal pain, high fever, and salmon-colored macules located mainly on the trunk. Histology demonstrates a lymphoplasmacytic inflammatory infiltrate and associated hemorrhage.

(Choice D) *Shigella flexneri* infection is characterized by sudden onset of severe abdominal cramping, bloody diarrhea, vomiting, and high fever. Cryptitis, ulcerations, and crypt abscesses are identified on histology.

(Choice E) *Vibrio cholerae* causes cholera, which manifests with sudden onset, voluminous, "rice water" diarrhea and vomiting. Histology typically remains normal.

**Educational objective:**

*Clostridium difficile* infection is associated with white, patchy pseudomembranes on the bowel mucosa. These pseudomembranes consist of a neutrophil-predominant inflammatory infiltrate, fibrin, bacteria, and necrotic epithelium. Patients may develop a nonobstructive colonic dilation known as toxic megacolon, which can lead to colonic perforation.





A 55-year-old man comes to the office due to swelling in his groin that he first noticed 2 weeks ago.

Physical examination shows a bulge above the inguinal ligament that increases in size when the patient is asked to cough. He is referred to a surgeon and scheduled to undergo elective laparoscopic hernia repair.

Which of the following landmarks will best aid the surgeon in distinguishing an indirect from a direct inguinal hernia?

- ☐ A. Femoral vein
- ☐ B. Inferior epigastric vessels
- ☐ C. Pectineal ligament
- ☐ D. Rectus muscle sheath
- ☐ E. Spermatic cord
- ☐ F. Transversalis fascia

Submit





A 55-year-old man comes to the office due to swelling in his groin that he first noticed 2 weeks ago.

Physical examination shows a bulge above the inguinal ligament that increases in size when the patient is asked to cough. He is referred to a surgeon and scheduled to undergo elective laparoscopic hernia repair.

Which of the following landmarks will best aid the surgeon in distinguishing an indirect from a direct inguinal hernia?

- ☐ A. Femoral vein (2%)
- ☒ B. Inferior epigastric vessels (84%)
- ☐ C. Pectineal ligament (1%)
- ☐ D. Rectus muscle sheath (1%)
- ☐ E. Spermatic cord (5%)
- ☐ F. Transversalis fascia (4%)

Correct



84%

Answered correctly



21 secs

Time Spent



11/01/2020

Last Updated

Block Time Remaining: 00:07:14

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Feedback



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End Block



Item 7 of 40

Question Id: 418



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

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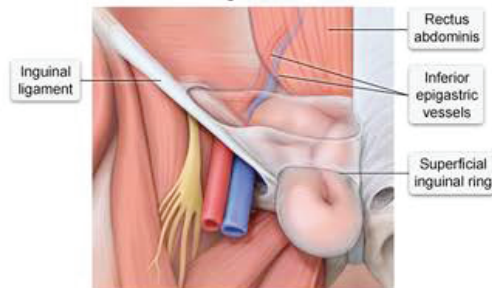
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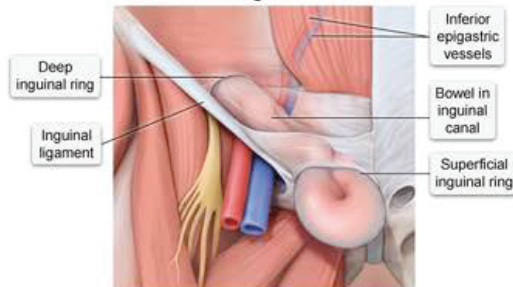
### Exhibit Display

#### Inguinal hernias

##### Direct inguinal hernia



##### Indirect inguinal hernia



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Block Time Remaining: 00:07:14

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**Inguinal hernias** are located above the inguinal ligament and are much more common in men. The **inferior epigastric vessels** are clearly visible on the anterior abdominal wall during laparoscopic hernia repair and can be used as a landmark to **distinguish** between direct and indirect inguinal hernias.

**Indirect** inguinal hernias occur due to failure of the processus vaginalis to obliterate, allowing abdominal contents to protrude **lateral** to the inferior epigastric vessels through the deep (internal) inguinal ring. The abdominal contents follow the path of the inguinal canal and may exit through the superficial (external) inguinal ring into the scrotum.

**Direct** inguinal hernias occur due to weakness in the transversalis fascia that allows abdominal contents to protrude **medial** to the inferior epigastric vessels into the **Hesselbach triangle**. Compared to indirect inguinal hernias, direct hernias are less prone to incarceration due to their wide neck. It is also uncommon for them to descend into the scrotum as there is no direct path through the abdominal fascia.

**(Choice A)** The femoral vein runs directly lateral to **femoral hernias**, which protrude below the inguinal ligament into the femoral canal.

**(Choice C)** The pectineal ligament (inguinal ligament of Cooper) forms the posterior border of the femoral ring and would be located behind a femoral hernia that protrudes through the ring.

**(Choice D)** The rectus abdominis muscle sheath forms the most medial aspect of the Hesselbach triangle.





Item 7 of 40

Question Id: 418



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



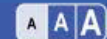
Notes



Calculator



Reverse Color



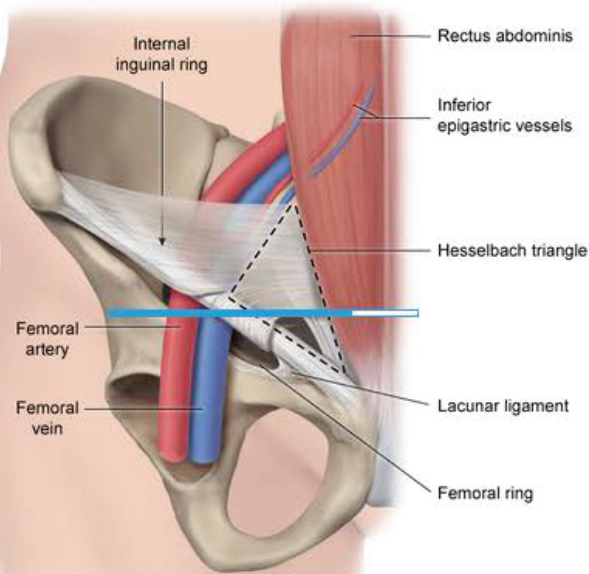
Text Zoom



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## Exhibit Display

## Groin hernias



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End Block



Item 7 of 40

Question Id: 418



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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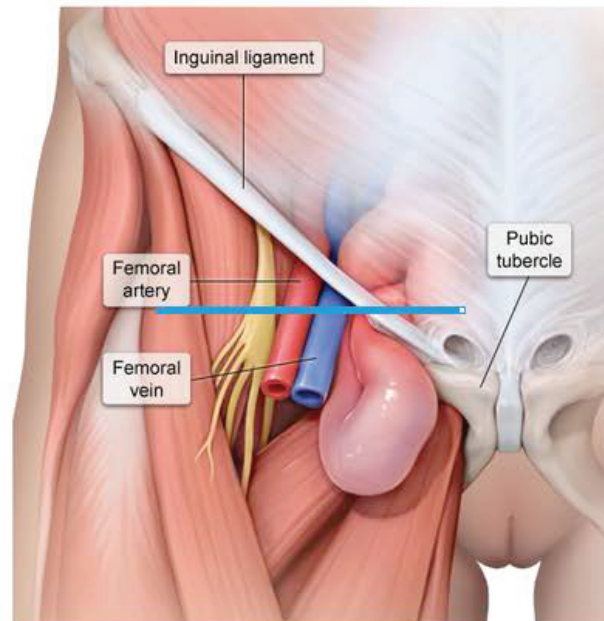
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## Exhibit Display

## Femoral hernia



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**(Choice C)** The pectineal ligament (inguinal ligament of Cooper) forms the posterior border of the femoral ring and would be located behind a femoral hernia that protrudes through the ring.

**(Choice D)** The rectus abdominis muscle sheath forms the most medial aspect of the Hesselbach triangle, which is the site of protrusion for direct inguinal hernias. Because both direct and indirect inguinal hernias lie lateral to the rectus abdominis muscle sheath, it would not be useful for distinguishing these two types of hernia.

**(Choice E)** Indirect inguinal hernias follow the path of the spermatic cord (or uterine round ligament) as it courses through the deep (internal) inguinal ring.

**(Choice F)** The transversalis fascia is the site of weakness in a direct inguinal hernia and lies posterior to indirect inguinal hernias as they extend through the inguinal canal.

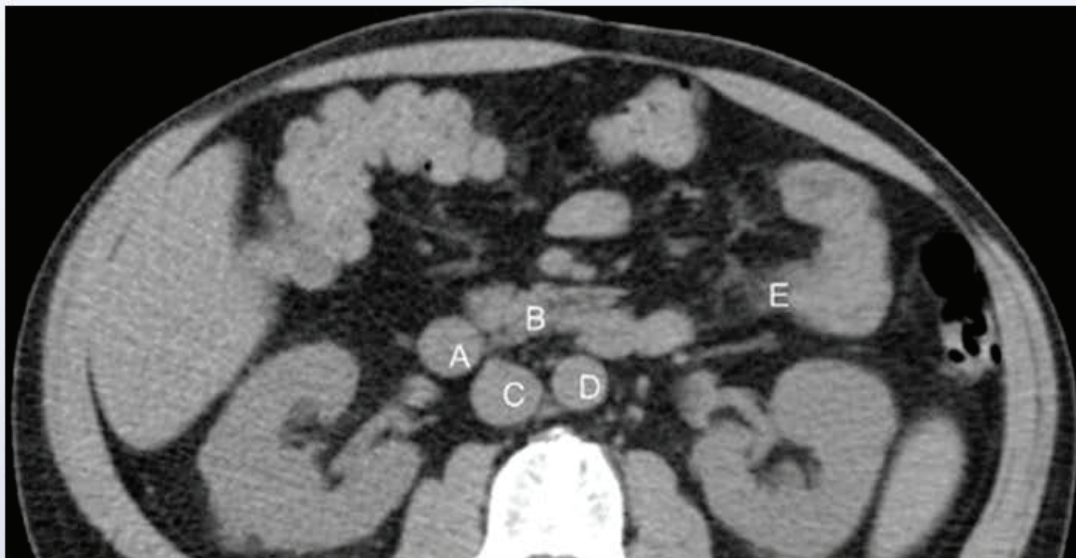
### Educational objective:

The inferior epigastric vessels are useful as a landmark during laparoscopic hernia repair to classify the type of inguinal hernia. Indirect inguinal hernias protrude through the deep inguinal ring into the inguinal canal lateral to the inferior epigastric vessels. In contrast, direct inguinal hernias protrude through Hesselbach's triangle medial to the inferior epigastric vessels.





A 48-year-old man is evaluated for abdominal pain and diarrhea. The patient characterizes his stool as voluminous and foul smelling. He has no significant past medical history. The patient drinks 6 cans of beer daily. On examination, he has normal bowel sounds and mild epigastric tenderness. A 72-hour stool collection shows excessive excretion of fecal fat. A CT scan of the abdomen is shown in the image below. Involvement of which of the following structures is most likely causing this patient's symptoms?





Item 8 of 40

Question Id: 1738



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

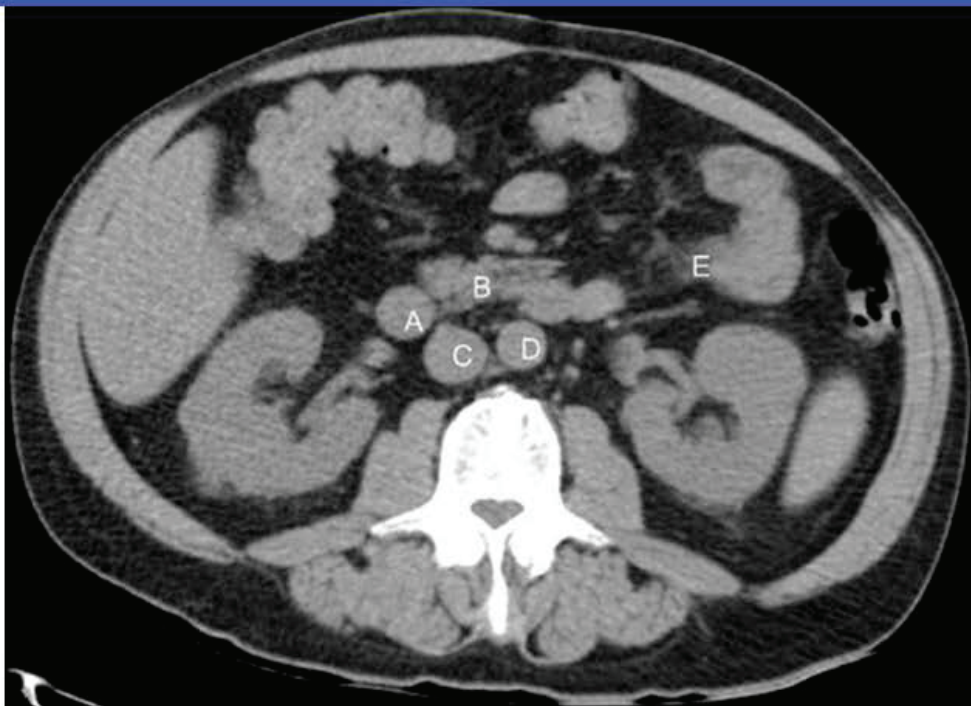


Text Zoom



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### Exhibit Display



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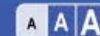
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☐ A.A☐ B.B☐ C.C☐ D.D☐ E.E**Submit**



- ☐ A.A (1%)
- ☒ B.B (91%)
- ☐ C.C (0%)
- ☐ D.D (0%)
- ☐ E.E (5%)

Correct



91%

Answered correctly



40 secs

Time spent



12/28/2020

Last updated

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

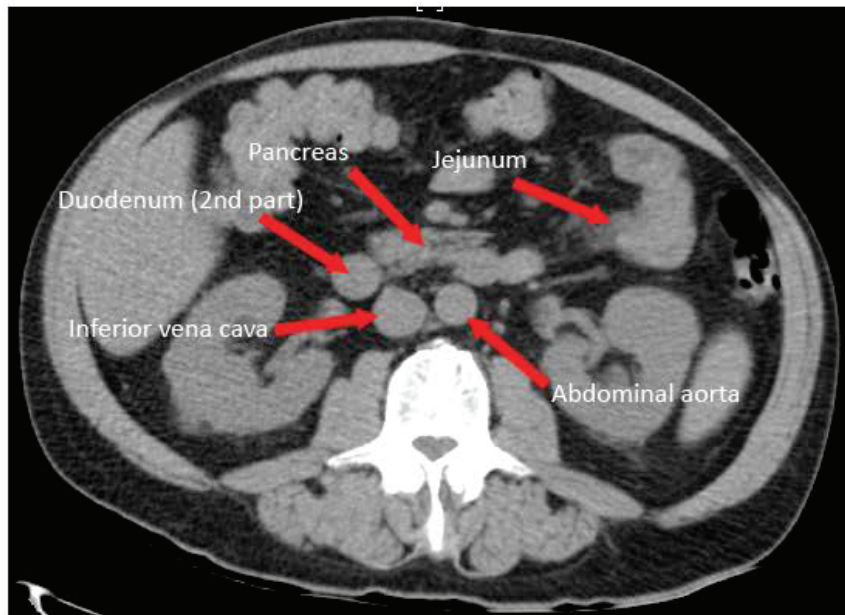


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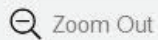


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The head, neck, and body of the pancreas are retroperitoneal, whereas the tail is peritoneal. The head of

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This patient with excessive alcohol use, **epigastric pain**, and **steatorrhea** likely has **chronic pancreatitis** with exocrine insufficiency. Atrophy and fibrosis of pancreatic acinar cells result in failed secretion of adequate amounts of digestive enzymes (eg, lipase). Consequently, patients may develop **fat malabsorption** with greasy, malodorous stools that are difficult to flush. A 72-hour stool collection can confirm excessive excretion of fecal fat.

The head, neck, and body of the **pancreas** are retroperitoneal, whereas the tail is peritoneal. The head of the pancreas lies in the curve of the duodenum and overlies the L2 vertebra, with a portion extending behind the superior mesenteric vessels (uncinate process). The neck connects the head to the body and lies anterior to the portal vein and superior mesenteric vessels. The pancreas body overlies the L1 and L2 vertebrae and makes contact posteriorly with the aorta, left adrenal gland, left kidney, and renal vessels. The tail of the pancreas courses within the splenorenal ligament alongside the splenic vessels.

**(Choice A)** This structure is the second (descending) part of the duodenum.

**(Choice C)** This structure is the inferior vena cava, which lies on the right side of the vertebrae in a retroperitoneal position.

**(Choice D)** This structure is the abdominal aorta, which lies on the left side of the vertebrae in a





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



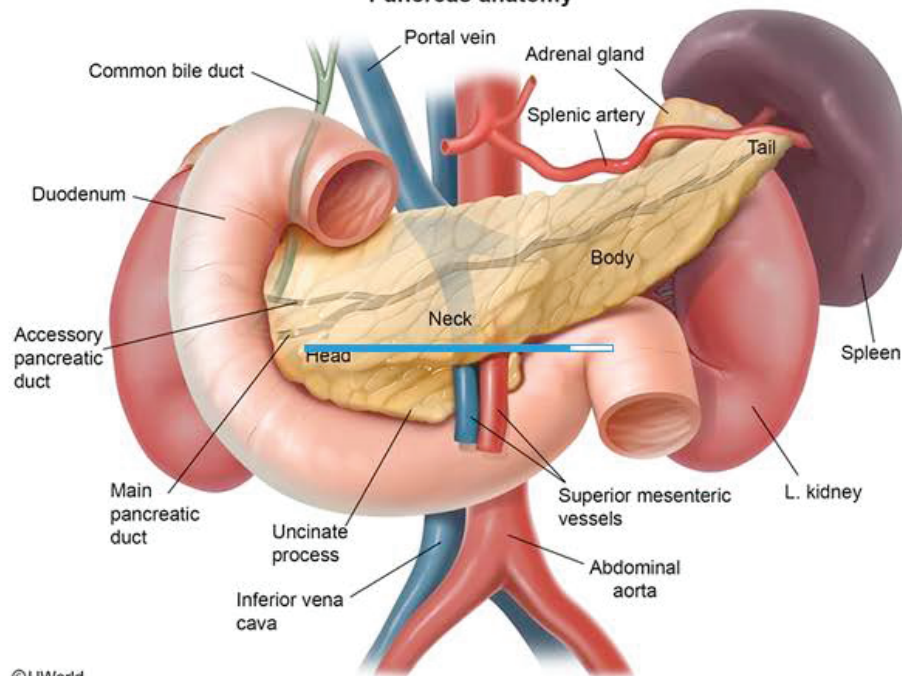
Text Zoom



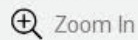
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## Exhibit Display

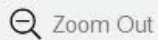
## Pancreas anatomy



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**(Choice A)** This structure is the second (descending) part of the duodenum.

**(Choice C)** This structure is the inferior vena cava, which lies on the right side of the vertebrae in a retroperitoneal position.

**(Choice D)** This structure is the abdominal aorta, which lies on the left side of the vertebrae in a retroperitoneal position.

**(Choice E)** At this level in the abdominal cavity, these loops of small bowel represent jejunum. If this CT slice were lower in the abdomen, these loops would more likely represent ileum.

### Educational objective:

Chronic pancreatitis often presents with epigastric pain and pancreatic exocrine insufficiency resulting in fat malabsorption/steatorrhea. On abdominal CT scan, the pancreas can be identified by its head in close association with the second part of the duodenum; its body overlying the aorta, left kidney, and renal vessels; and its tail lying within the splenorenal ligament.

### References

- [Chronic pancreatitis.](#)







A 32-year-old man is being evaluated due to several weeks of watery diarrhea. He has also had intermittent, crampy abdominal pain and has lost 7 kg (15.4 lb) during this period. The patient has a history of HIV and was hospitalized 6 months ago for *Pneumocystis* pneumonia. On physical examination, the patient is afebrile, and the abdomen is soft and nontender with no organomegaly. Stool tests for leukocytes and occult blood are negative. Endoscopy is performed, and mucosal biopsy shows an inflammatory infiltrate in the lamina propria and pathogens lining the epithelium, as shown in the [exhibit](#). The organisms have a cystic appearance on modified acid-fast staining. Which of the following is the most likely cause of this patient's condition?

- ☐ A. *Clostridium difficile*
- ☐ B. *Cryptosporidium parvum*
- ☐ C. *Entamoeba histolytica*
- ☐ D. Enteropathogenic *Escherichia coli*
- ☐ E. *Giardia lamblia*
- ☐ F. *Mycobacterium avium* complex





intermittent, crampy abdominal pain and has lost 7 kg (15.4 lb) during this period. The patient has a history of HIV and was hospitalized 6 months ago for *Pneumocystis* pneumonia. On physical examination, the patient is afebrile, and the abdomen is soft and nontender with no organomegaly. Stool tests for leukocytes and occult blood are negative. Endoscopy is performed, and mucosal biopsy shows an inflammatory infiltrate in the lamina propria and pathogens lining the epithelium, as shown in the [exhibit](#). The organisms have a cystic appearance on modified acid-fast staining. Which of the following is the most likely cause of this patient's condition?

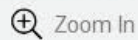
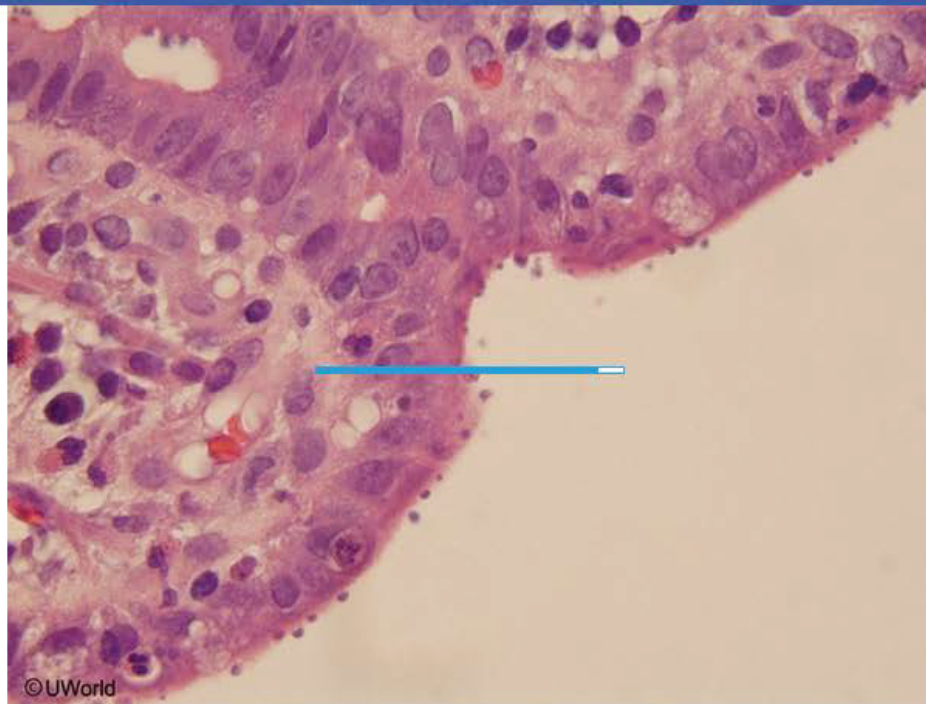
- ☐ A. *Clostridium difficile*
- ☐ B. *Cryptosporidium parvum*
- ☐ C. *Entamoeba histolytica*
- ☐ D. Enteropathogenic *Escherichia coli*
- ☐ E. *Giardia lamblia*
- ☐ F. *Mycobacterium avium* complex
- ☐ G. *Salmonella enteritidis*



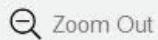


Intermittent, crampy abdominal pain and has lost 7 kg (15.4 lb) during this period. The patient has a history

## Exhibit Display



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End Block





intermittent, crampy abdominal pain and has lost 7 kg (15.4 lb) during this period. The patient has a history of HIV and was hospitalized 6 months ago for *Pneumocystis* pneumonia. On physical examination, the patient is afebrile, and the abdomen is soft and nontender with no organomegaly. Stool tests for leukocytes and occult blood are negative. Endoscopy is performed, and mucosal biopsy shows an inflammatory infiltrate in the lamina propria and pathogens lining the epithelium, as shown in the [exhibit](#). The organisms have a cystic appearance on modified acid-fast staining. Which of the following is the most likely cause of this patient's condition?

- ☐ A. *Clostridium difficile*
- ☐ B. *Cryptosporidium parvum*
- ☐ C. *Entamoeba histolytica*
- ☐ D. Enteropathogenic *Escherichia coli*
- ☐ E. *Giardia lamblia*
- ☐ F. *Mycobacterium avium* complex
- ☐ G. *Salmonella enteritidis*





patient is afebrile, and the abdomen is soft and nontender with no organomegaly. Stool tests for leukocytes and occult blood are negative. Endoscopy is performed, and mucosal biopsy shows an inflammatory infiltrate in the lamina propria and pathogens lining the epithelium, as shown in the [exhibit](#). The organisms have a cystic appearance on modified acid-fast staining. Which of the following is the most likely cause of this patient's condition?

- ☐ A. *Clostridium difficile* (4%)
- ☒ B. *Cryptosporidium parvum* (70%)
- ☐ C. *Entamoeba histolytica* (3%)
- ☐ D. Enteropathogenic *Escherichia coli* (0%)
- ☐ E. *Giardia lamblia* (4%)
- ☐ F. *Mycobacterium avium* complex (14%)
- ☐ G. *Salmonella enteritidis* (1%)

Correct

70%



23 secs



11/16/2020

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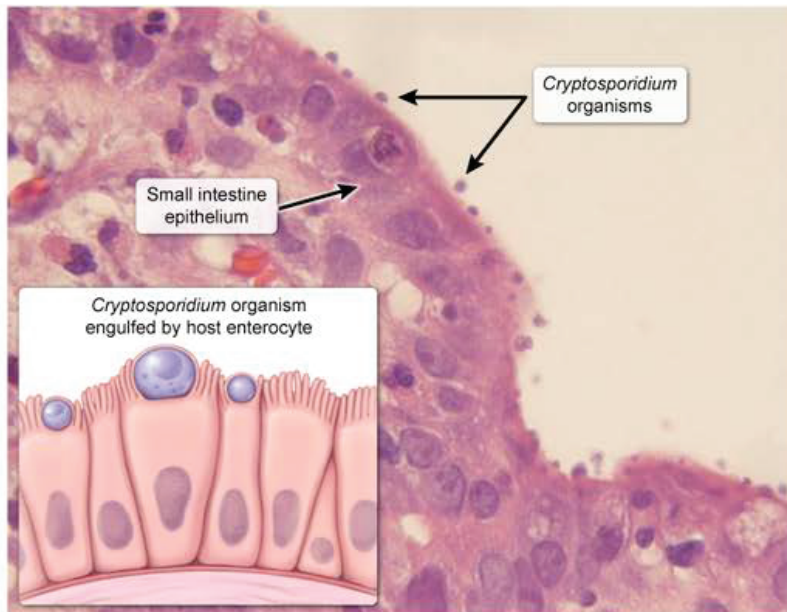


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## Cryptosporidiosis



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***Cryptosporidium*** is a protozoal organism that is a common cause of infectious diarrhea. Oocysts are ingested in contaminated food or water, travel to the small intestine, and shed sporozoites that attach to the **epithelial cells**. Individuals who are otherwise healthy often develop self-limited, **watery (secretory) diarrhea**. However, those with impaired cell-mediated immunity—particularly individuals with **advanced AIDS** (as is likely in this patient with HIV who recently had *Pneumocystis pneumonia*)—are at risk for life-threatening diarrhea with fluid loss of >20 L per day.

Standard ova and parasite stool tests usually cannot detect the organism, and fecal leukocytes/occult blood tests are generally negative (because the pathogen does not cause inflammatory diarrhea). However, the diagnosis can often be made by modified **acid-fast stain** of the stool, which usually reveals **ooocysts**. Histopathology generally shows **villous blunting**, an inflammatory infiltrate in the lamina propria, and **basophilic *Cryptosporidium* organisms** on the brush border of the mucosal surface.

**(Choice A)** *Clostridium difficile* is a gram-positive, spore-forming bacterium that causes toxin-mediated inflammatory colitis (usually with fecal leukocytes/blood). It is not acid-fast or cystic.

**(Choice C)** *Entamoeba histolytica* is an ameba that causes dysentery (bloody diarrhea). Histopathology generally reveals flask-shaped colonic ulcers with "foamy" **trophozoites** that resemble macrophages.

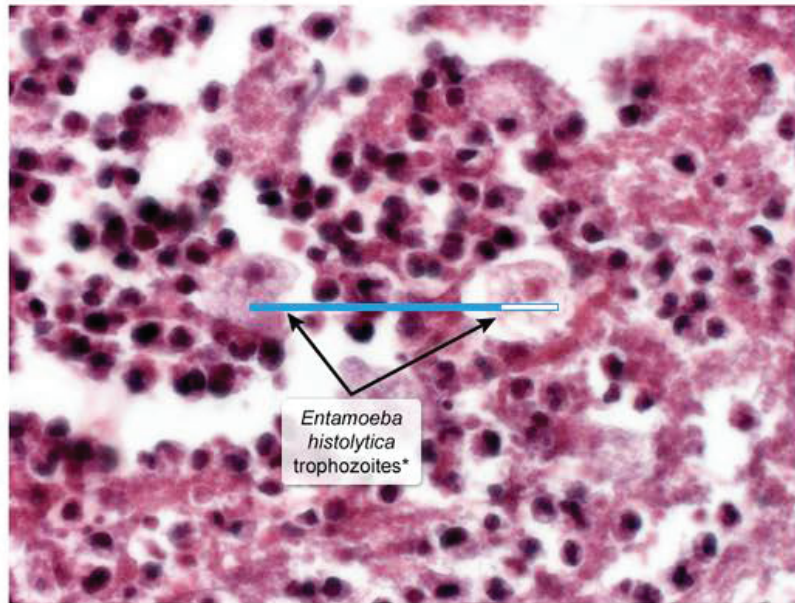
**(Choice D)** Enteropathogenic *Escherichia coli* attaches to and effaces the small bowel epithelium, leading





## Exhibit Display

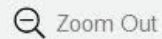
## Amebiasis



*Entamoeba  
histolytica*  
trophozoites\*

\*Vacuolated cytoplasm with ingested erythrocytes.

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**(Choice D)** Enteropathogenic *Escherichia coli* attaches to and effaces the small bowel epithelium, leading to watery, noninflammatory (no blood or leukocytes) diarrhea. However, this pathogen is a gram-negative rod, not an acid-fast cyst.

**(Choice E)** *Giardia lamblia* is a protozoal organism that classically causes foul-smelling, greasy diarrhea and excessive flatulence after consumption of contaminated water. Stool microscopy generally shows oval/ellipsoid cysts or **pear-shaped trophozoites**; they are not acid-fast.

**(Choice F)** *Mycobacterium avium* complex is a common opportunistic infection in patients with advanced AIDS (CD4 count  $<50/\text{mm}^3$ ) and often presents with diarrhea and weight loss. It is marked by **acid-fast bacilli** within macrophages.

**(Choice G)** *Salmonella enteritis* is a common food-borne infection and usually presents with acute, self-limited diarrhea, vomiting, fever, and abdominal cramping. It is a gram-negative bacillus, not an acid-fast cyst.

**Educational objective:**

*Cryptosporidium* is a common cause of self-limited diarrhea in immunocompetent hosts, but may cause life-threatening diarrhea in immunocompromised patients (eg, advanced AIDS). Diagnosis may be made by visualizing oocysts with modified acid-fast stain in stool or basophilic organisms lining the brush-border in a







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

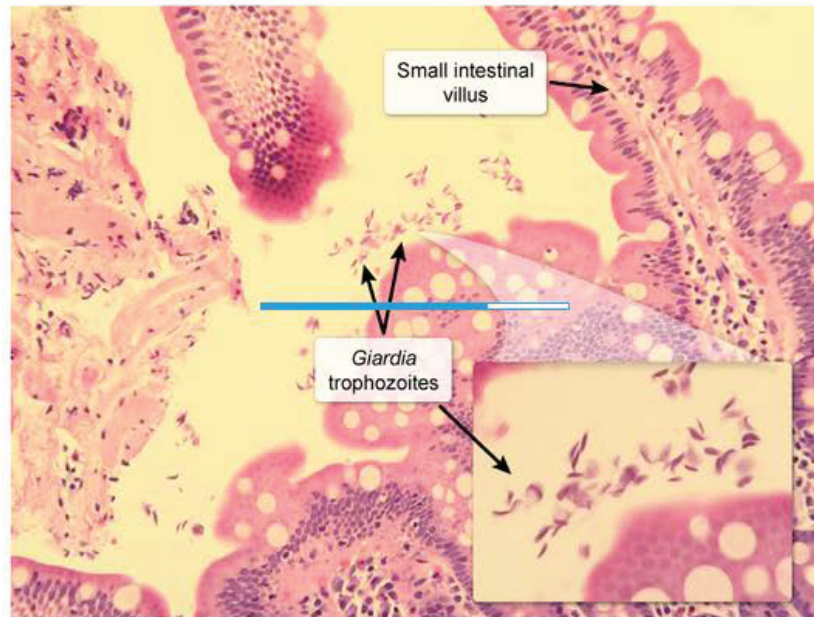
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(Choice D) Enteropathogenic *Escherichia coli* attaches to and effaces the small bowel epithelium, leading

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## Giardiasis



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1



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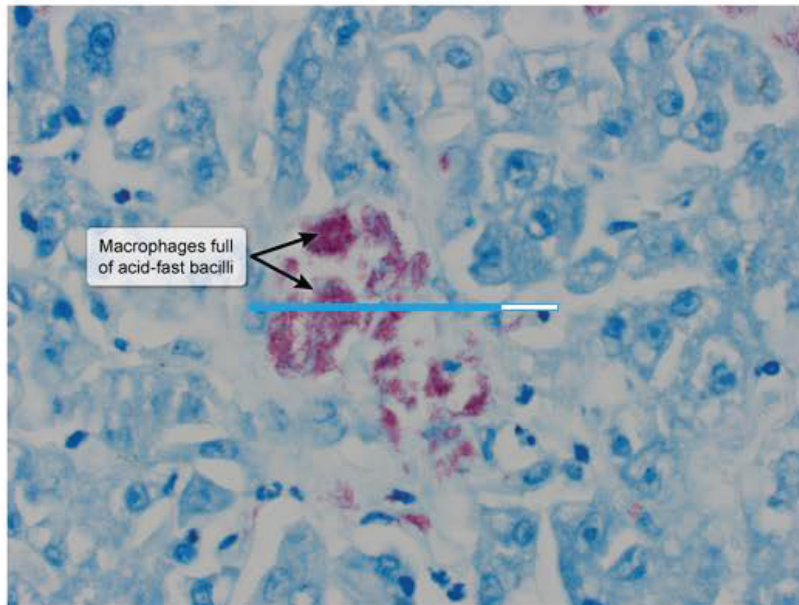
End Block



(Choice D) Enteropathogenic *Escherichia coli* attaches to and effaces the small bowel epithelium, leading

### Exhibit Display

#### *Mycobacterium avium* complex (MAC)



Acid fast stain

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rod, not an acid-fast cyst.

**(Choice E)** *Giardia lamblia* is a protozoal organism that classically causes foul-smelling, greasy diarrhea and excessive flatulence after consumption of contaminated water. Stool microscopy generally shows oval/ellipsoid cysts or **pear-shaped trophozoites**; they are not acid-fast.

**(Choice F)** *Mycobacterium avium* complex is a common opportunistic infection in patients with advanced AIDS (CD4 count  $<50/\text{mm}^3$ ) and often presents with diarrhea and weight loss. It is marked by **acid-fast bacilli** within macrophages.

**(Choice G)** *Salmonella enteritis* is a common food-borne infection and usually presents with acute, self-limited diarrhea, vomiting, fever, and abdominal cramping. It is a gram-negative bacillus, not an acid-fast cyst.

**Educational objective:**

*Cryptosporidium* is a common cause of self-limited diarrhea in immunocompetent hosts, but may cause life-threatening diarrhea in immunocompromised patients (eg, advanced AIDS). Diagnosis may be made by visualizing oocysts with modified acid-fast stain in stool or basophilic organisms lining the brush-border in a biopsy.







A 46-year-old homeless man comes to the emergency department with fever and chest pain that worsens with swallowing. The patient has been hospitalized several times recently with *Pneumocystis jirovecii* pneumonia. He has a history of intravenous drug use. His temperature is 37.8 C (100 F). Oropharyngeal examination is remarkable only for poor dentition. Esophagogastroduodenoscopy is performed and reveals esophageal hyperemia and linear ulcerations. Which of the following is the most likely cause of this patient's condition?

- ☐ A. *Babesia microti*
- ☐ B. *Cryptococcus neoformans*
- ☐ C. Cytomegalovirus
- ☐ D. *Isospora belli*
- ☐ E. *Toxoplasma gondii*
- ☐ F. *Trypanosoma cruzi*
- ☐ G. Varicella zoster virus





with swallowing. The patient has been hospitalized several times recently with *Pneumocystis jirovecii* pneumonia. He has a history of intravenous drug use. His temperature is 37.8 C (100 F). Oropharyngeal examination is remarkable only for poor dentition. Esophagogastroduodenoscopy is performed and reveals esophageal hyperemia and linear ulcerations. Which of the following is the most likely cause of this patient's condition?

- ☐ A. *Babesia microti* (2%)
- ☐ B. *Cryptococcus neoformans* (5%)
- ☒ C. Cytomegalovirus (77%)
- ☐ D. *Isospora belli* (3%)
- ☐ E. *Toxoplasma gondii* (2%)
- ☐ F. *Trypanosoma cruzi* (7%)
- ☐ G. *Varicella-zoster virus* (1%)

Correct

77%

01 min, 07 secs

02/04/2021

Block Time Remaining: 00:09:24

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End Block



### HIV-associated esophagitis

Pathogen	Endoscopic findings	Microscopic findings
<b><i>Candida albicans</i></b>	Patches of adherent, gray/white <b>pseudomembranes</b> on erythematous mucosa	<b>Yeast</b> cells & pseudohyphae invading mucosal cells
<b>HSV-1</b>	Small <b>vesicles</b> → "punched-out" ulcers	Eosinophilic intranuclear inclusions ( <b>Cowdry type A</b> ) in multinuclear squamous cells at ulcer margins
<b>CMV</b>	<b>Linear</b> ulcerations	Intranuclear & cytoplasmic <b>inclusions</b>

**CMV** = cytomegalovirus; **HSV** = herpes simplex virus.







*Pneumocystis jirovecii* affects almost exclusively immunocompromised individuals; therefore, it is likely that this patient has HIV. He has now developed the painful swallowing characteristic of **esophagitis**. The 3 main causes of HIV-associated esophagitis are *Candida* (most common), cytomegalovirus (CMV), and herpes simplex virus (HSV). All can manifest as dysphagia (difficulty swallowing) and/or odynophagia (pain on swallowing) and can be difficult to distinguish clinically; however, accurate diagnosis is essential for treatment. **CMV esophagitis** is typically characterized endoscopically by **large, shallow linear ulcerations** (most commonly in the distal esophagus) with intranuclear and cytoplasmic inclusions seen microscopically.

**(Choice A)** *Babesia microti* is transmitted by a tick bite and causes babesiosis. It is endemic in the northeastern United States and manifests with flulike symptoms, hepatosplenomegaly, and anemia. It often affects asplenic patients.

**(Choice B)** *Cryptococcosis* causes meningitis (not esophagitis) in patients with HIV.

**(Choice D)** *Isospora belli* causes profuse watery diarrhea in patients with HIV. It has no role in the development of esophagitis.

**(Choice E)** In patients with HIV, *Toxoplasma gondii* causes ring-enhancing brain lesions and chorioretinitis.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

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northeastern United States and manifests with flulike symptoms, hepatosplenomegaly, and anemia. It often affects asplenic patients.

**(Choice B)** *Cryptococcosis* causes meningitis (not esophagitis) in patients with HIV.

**(Choice D)** *Isospora belli* causes profuse watery diarrhea in patients with HIV. It has no role in the development of esophagitis.

**(Choice E)** In patients with HIV, *Toxoplasma gondii* causes ring-enhancing brain lesions and chorioretinitis.

**(Choice F)** *Trypanosoma cruzi* causes Chagas disease (American trypanosomiasis). Chronic disease leads to cardiomyopathy, achalasia, megacolon, and megaureter.

**(Choice G)** HSV, not varicella zoster virus (VZV), causes esophagitis in patients with HIV. VZV causes chickenpox (varicella) and shingles (zoster).

### Educational objective:

Infectious esophagitis is common in patients with HIV. The most common cause is *Candida albicans*, although cytomegalovirus and herpes simplex virus are also frequently implicated. Diagnosis is based on endoscopic and microscopic findings.

Microbiology

Gastrointestinal &amp; Nutrition

Esophagitis

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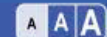
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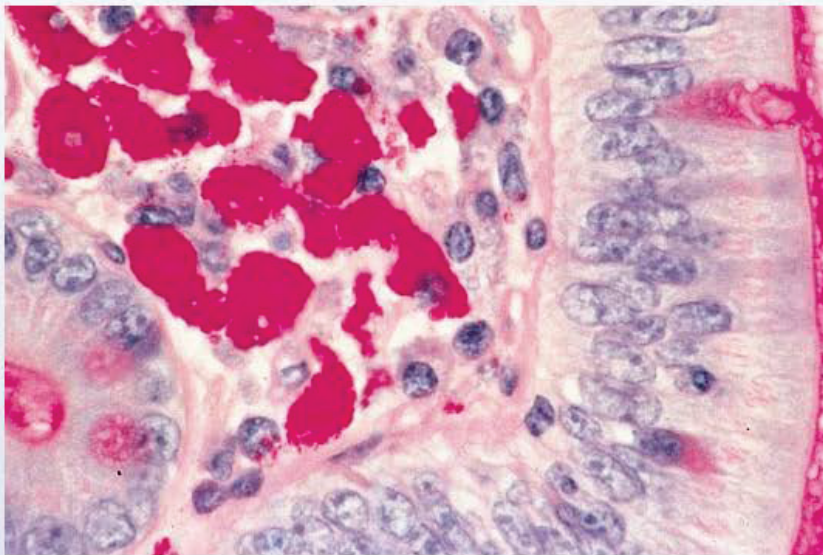
Suspend



End Block



A 46-year-old Caucasian male is being worked up for abdominal discomfort, loose stool and recent weight loss. Intestinal biopsy is performed and periodic acid-Schiff (PAS) reaction is used on the sample (see the slide below).

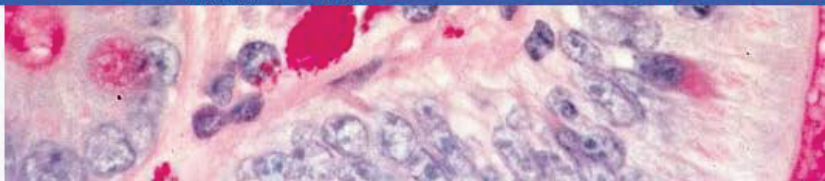


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The intense pink discoloration demonstrated on the slide most likely indicates the presence of:







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The intense pink discoloration demonstrated on the slide most likely indicates the presence of:

- ☐ A. Peroxidase
- ☐ B. Calcium
- ☐ C. Iron
- ☐ D. Neutral lipid
- ☐ E. Glycoprotein
- ☐ F. Alkaline phosphatase

Submit





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The intense pink discoloration demonstrated on the slide most likely indicates the presence of:

- ☐ A. Peroxidase (15%)
- ☐ B. Calcium (2%)
- ☐ C. Iron (6%)
- ☐ D. Neutral lipid (14%)
- ☒ E. Glycoprotein (57%)
- ☐ F. Alkaline phosphatase (3%)

Correct

57%



13 secs



01/30/2021

Block Time Remaining: 00:09:37

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Feedback



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End Block



The periodic acid-Schiff (PAS) reaction is used in histochemical staining because the periodic acid oxidizes carbon-carbon bonds, forming aldehydes that produce a brilliant magenta color upon reacting with the fuchsin-sulfurous acid. As a result, the PAS stain is particularly effective at highlighting polysaccharides of the fungal cell wall, mucosubstances secreted by epithelia, and basement membranes. Diastase can be used in conjunction with PAS to demonstrate glycogen, which is found in skin, liver, parathyroid, and skeletal/cardiac muscle. The diastase works by digesting glycogen to form maltose and glucose, two sugars that are easily washed from sections during processing (therefore giving a negative reaction).

The glycoprotein present in the cell walls of the gram-positive actinomycete *Tropheryma whippelii* appears magenta with PAS and is diastase-resistant, which makes this stain an excellent choice when microscopically evaluating small bowel mucosa for Whipple disease.

**(Choice A)** Peroxidase staining can be used to differentiate subtypes of acute leukemia, and horseradish peroxidase is useful in immunoblotting (eg, Western blot).

**(Choice B)** Calcium appears as a dark purple deposit on hematoxylin and eosin stain.

**(Choice C)** Iron appears blue with stains such as Prussian blue.

**(Choice D)** Neutral lipids can be identified with a multitude of stains, including Nile red or Sudan black (with







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

The glycoprotein present in the cell walls of the gram-positive actinomycete *Tropheryma whippelii* appears magenta with PAS and is diastase-resistant, which makes this stain an excellent choice when microscopically evaluating small bowel mucosa for Whipple disease.

**(Choice A)** Peroxidase staining can be used to differentiate subtypes of acute leukemia, and horseradish peroxidase is useful in immunoblotting (eg, Western blot).

**(Choice B)** Calcium appears as a dark purple deposit on hematoxylin and eosin stain.

**(Choice C)** Iron appears blue with stains such as Prussian blue.

**(Choice D)** Neutral lipids can be identified with a multitude of stains, including Nile red or Sudan black (with the latter being useful for frozen sections).

**(Choice F)** Alkaline phosphatase is an enzyme marker of osteoblasts. Staining with this enzyme can be helpful in identifying bone tumors.

### Educational Objective:

The glycoprotein in the cell walls of the actinomycete *Tropheryma whippelii* colors magenta with PAS and is diastase-resistant, making this stain an excellent choice in evaluating tissue for Whipple disease.

Pathology

Gastrointestinal &amp; Nutrition

Whipple disease

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Feedback



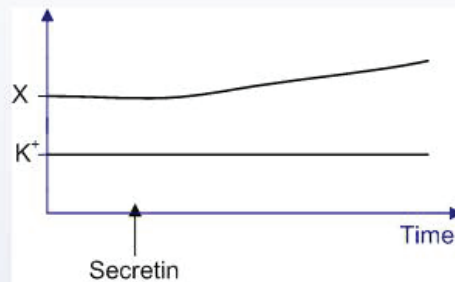
Suspend



End Block



In an animal experiment, the pancreatic duct is cannulated and different secretory stimuli are applied to the gland. The following tracings are obtained by measuring pancreatic fluid constituents:



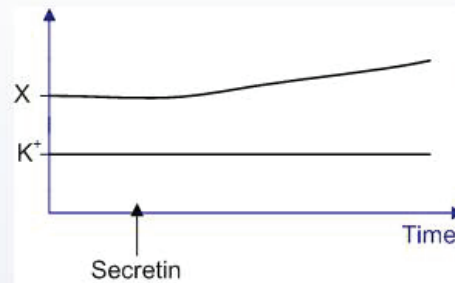
Substance 'X' is most likely which of the following?

- ☐ A. Sodium
- ☐ B. Chloride
- ☐ C. Trypsinogen
- ☒ D. Bicarbonate
- ☐ E. Phosphate





gland. The following tracings are obtained by measuring pancreatic fluid constituents:



Substance 'X' is most likely which of the following?

- ☐ A. Sodium (1%)
- ☐ B. Chloride (3%)
- ☐ C. Trypsinogen (13%)
- ☒ D. Bicarbonate (80%)
- ☐ E. Phosphate (0%)





Secretin is a hormone produced by duodenal S-cells and released in response to increased duodenal  $\text{H}^+$  concentrations. Secretin stimulates pancreatic ductal cells to increase bicarbonate secretion in order to neutralize the acidity of the gastric contents entering the duodenum. Remember that pancreatic juice is an isotonic secretion, which normally contains  $\text{Na}^+$  and  $\text{K}^+$  in the same concentrations as found in plasma, a higher  $\text{HCO}_3^-$  concentration than in plasma and a lower  $\text{Cl}^-$  concentration than in plasma. As pancreatic juice flow rates and secretin stimulation increase, the concentration of  $\text{HCO}_3^-$  increases and the concentration of  $\text{Cl}^-$  decreases.

**(Choice A)** Regardless of flow rate or hormonal stimulation, the sodium concentration of pancreatic secretions is identical to that of plasma.

**(Choice B)** The chloride content of pancreatic secretions decreases as the bicarbonate content increases, because chloride and bicarbonate are exchanged for one another at the apical surfaces of pancreatic ductal cells.

**(Choice C)** Trypsinogen is a pancreatic proenzyme that is converted to its active form, trypsin, by enterokinase in the intestinal brush border. Active trypsin can also activate trypsinogen. Cholecystokinin



secretions is identical to that of plasma.

**(Choice B)** The chloride content of pancreatic secretions decreases as the bicarbonate content increases, because chloride and bicarbonate are exchanged for one another at the apical surfaces of pancreatic ductal cells.

**(Choice C)** Trypsinogen is a pancreatic proenzyme that is converted to its active form, trypsin, by enterokinase in the intestinal brush border. Active trypsin can also activate trypsinogen. Cholecystokinin and cholinergic stimulation increase the secretion of pancreatic enzymes.

**(Choice E)** Phosphate secretion is not regulated in the pancreas.

### Educational Objective:

Duodenal S-cells secrete secretin in response to increasing  $H^+$  concentrations. Secretin increases pancreatic bicarbonate secretion. The chloride content of pancreatic secretions decreases in proportion to bicarbonate concentration increases.

Physiology

Gastrointestinal & Nutrition

Pancreas physiology

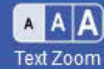
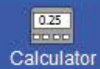
Subject

System

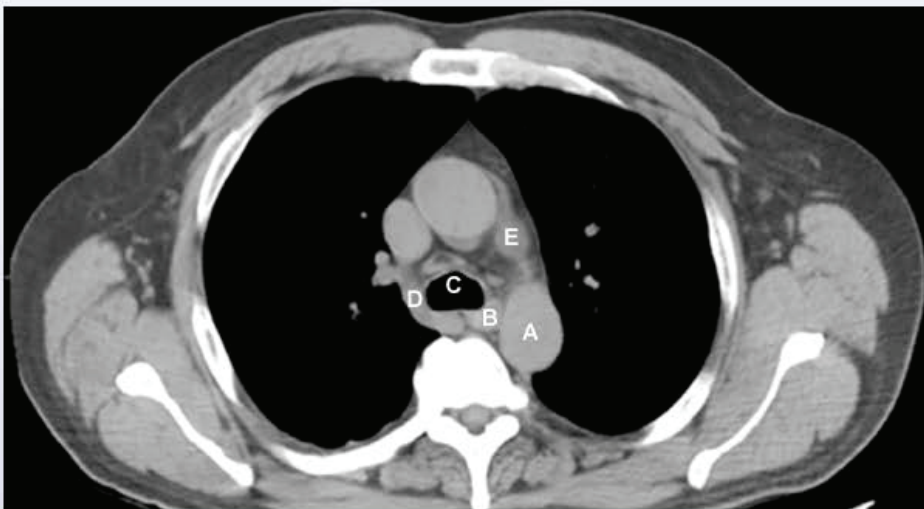
Topic

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A 47-year-old man comes to the office due to dysphagia. The patient says that it feels like food has been getting stuck in his throat over the last month. He has changed his diet to accommodate his symptoms and now consumes only liquid foods. The patient has a long history of postprandial heartburn that sometimes awakens him from sleep. He has treated his heartburn with over-the-counter antacids but usually only has partial relief. A thoracic CT image near the level of the aortic arch is shown below. This patient's symptoms are most likely related to pathology involving which of the following structures?







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



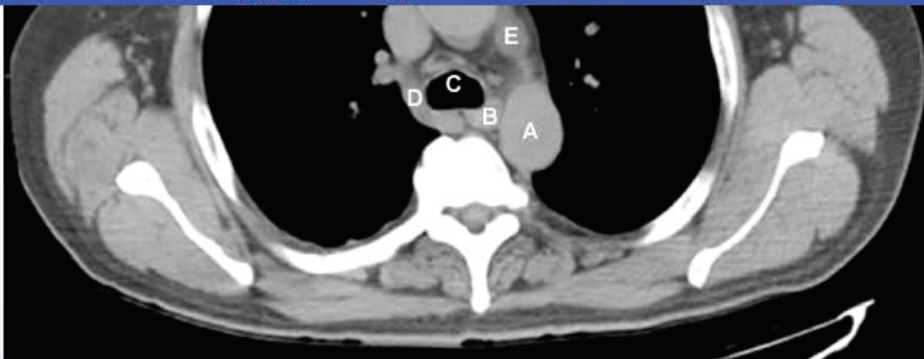
Reverse Color



Text Zoom



Settings



- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings



- ☐ A.A (3%)
- ☒ B.B (56%)
- ☐ C.C (26%)
- ☐ D.D (8%)
- ☐ E.E (4%)

Correct

56%  
Answered correctly

35 secs  
Time Spent

11/01/2020  
Last Updated

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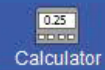
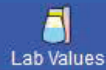
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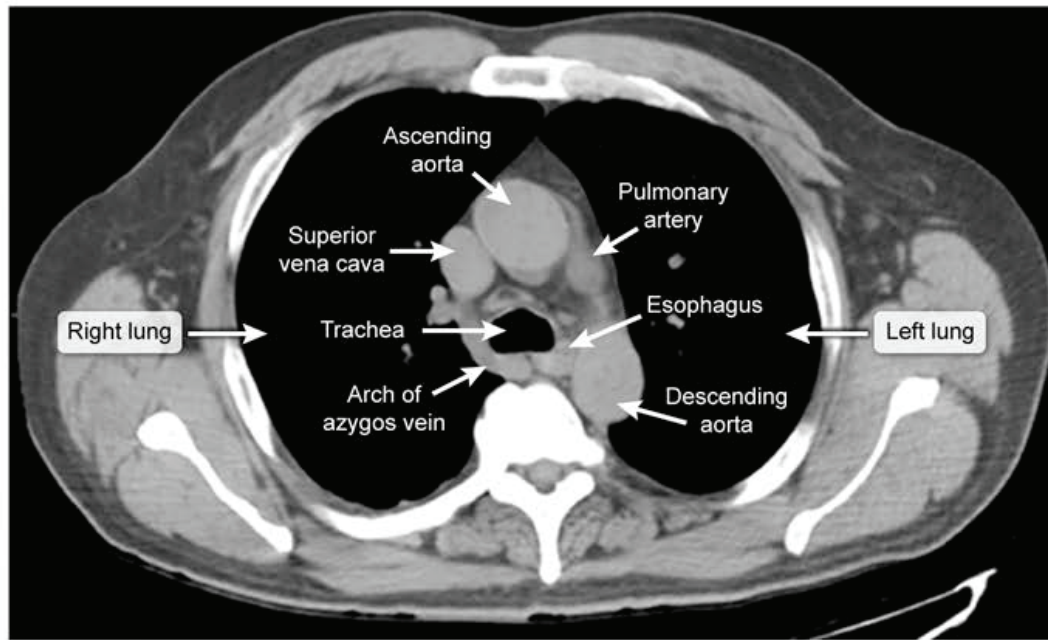
Feedback

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End Block



### Chest CT



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This patient's prolonged history of heartburn is suggestive of **gastroesophageal reflux disease** (GERD), a







©UWorld

This patient's prolonged history of heartburn is suggestive of **gastroesophageal reflux disease** (GERD), a condition that affects the esophagus. **Dysphagia** (ie, difficulty swallowing) is common in patients with longstanding GERD and can be caused by impaired peristalsis, esophageal inflammation/stricture, or malignancy.

In the thorax, the **esophagus** courses between the **trachea and vertebral bodies** and is typically collapsed with **no visible lumen**. The trachea serves as a good landmark because the radiolucency of the air in this structure allows one to differentiate it from the esophagus posteriorly and the great vessels anteriorly (**Choice C**).

(**Choice A**) This is the descending aorta.

(**Choice D**) This is the arch of the azygos vein as it curves over the right main bronchus to join with the superior vena cava. The azygos vein itself ascends along the thoracic vertebral column to the right of the esophagus.

(**Choice E**) This is a section of the top of the pulmonary artery as it passes underneath the aortic arch.

**Educational objective:**





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(**Choice E**) This is a section of the top of the pulmonary artery as it passes underneath the aortic arch.

### Educational objective:

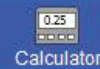
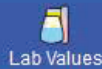
The esophagus is located between the trachea and the vertebral bodies in the superior thorax. It is typically collapsed with no visible lumen on CT images of the chest.

Anatomy

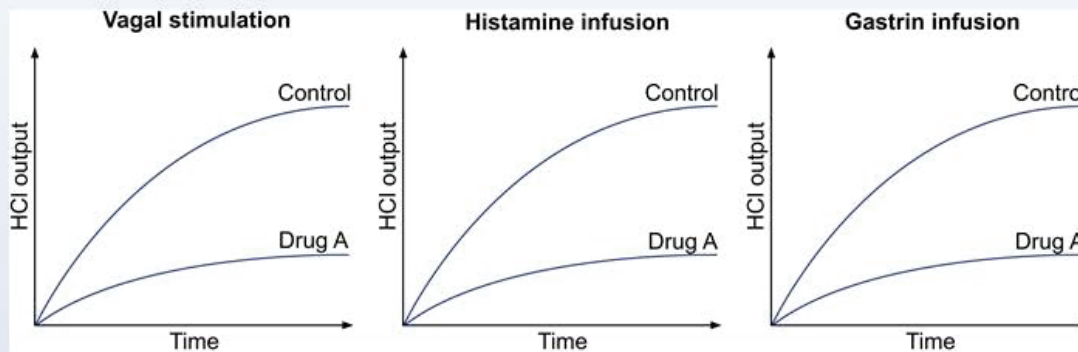
Gastrointestinal & Nutrition

Gastroesophageal reflux disease





A new medication, drug A, is being developed for the treatment of peptic ulcer disease. During initial testing, gastric acid secretion in experimental animals is stimulated by vagal stimulation, histamine infusion, or gastrin infusion. Before the stimulus is administered, the animals are divided into 2 groups, one group receives pretreatment with drug A, and the second one serves as the control and is given an injection of an equivalent volume of normal saline. The effects of the drug on hydrochloric acid (HCl) output by the stomach mucosa are recorded and shown in the graphs below.

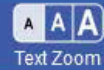
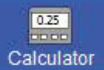


Drug A is most similar to which of the following medications?

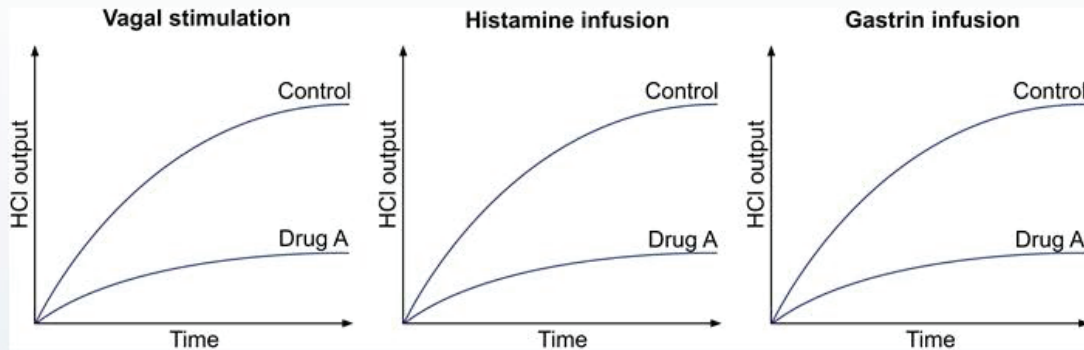
☐ A. Atropine







stomach mucosa are recorded and shown in the graphs below.



Drug A is most similar to which of the following medications?

- ☐ A. Atropine
- ☐ B. Bethanechol
- ☐ C. Cimetidine
- ☐ D. Lansoprazole
- ☐ E. Sucralfate





Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



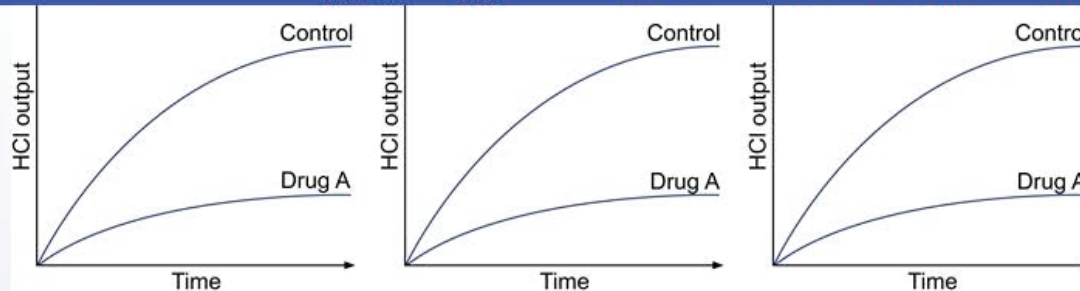
Reverse Color



Text Zoom



Settings



Drug A is most similar to which of the following medications?

- ☐ A. Atropine (10%)
- ☐ B. Bethanechol (2%)
- ☐ C. Cimetidine (10%)
- ☒ D. Lansoprazole (73%)
- ☐ E. Sucralfate (2%)

Correct

73%

19 secs

12/12/2020

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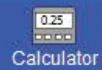
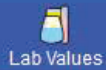
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Feedback

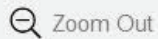
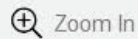
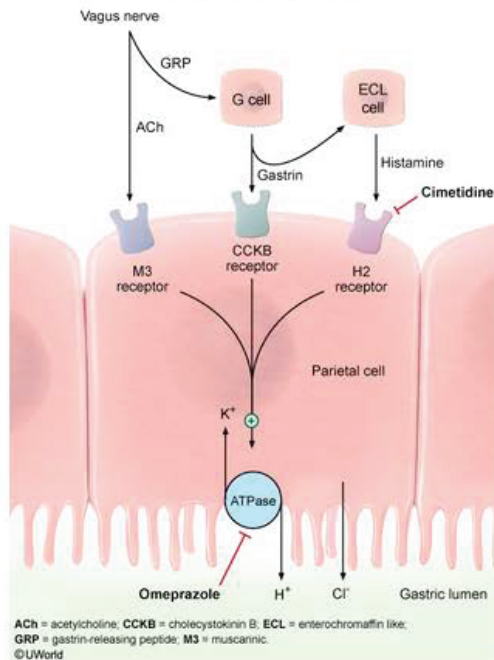
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### Exhibit Display

#### Parietal cell acid secretion







GRP = gastrin-releasing peptide; M3 = muscarinic.  
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Gastric **parietal cells** secrete **hydrochloric acid** (HCl) in response to 3 major stimulants: histamine, vagal output, and gastrin.

1. **Histamine** is released from enterochromaffin-like (ECL) cells and binds to H<sub>2</sub> receptors on the basolateral parietal cell membrane.
2. Vagal stimulation causes **acetylcholine** release, which directly stimulates HCl secretion by binding to parietal cell muscarinic (M<sub>3</sub>) receptors. In addition, vagal stimulation indirectly promotes HCl secretion via gastrin-releasing peptide (GRP), which stimulates gastrin release from G cells.
3. G cells also release **gastrin** in response to protein-rich meals. Gastrin primarily stimulates HCl secretion by binding to the CCK<sub>B</sub> receptor on ECL cells (promotes histamine release). It also directly binds to the CCK<sub>B</sub> receptor on parietal cells, but this mechanism is less significant for acid secretion.

The **final common pathway** for HCl secretion is the **H<sup>+</sup>/K<sup>+</sup>-ATPase proton pump**, located on the apical membrane of the parietal cell. Based on the graphs shown above, drug A inhibits gastric acid secretion in response to all 3 major stimulants. Therefore, drug A is most similar to a proton pump inhibitor (eg, **lansoprazole**, omeprazole) as it is likely inhibiting the H<sup>+</sup>/K<sup>+</sup>-ATPase proton pump.





**(Choice A)** Atropine is a nonselective antimuscarinic agent often used to produce mydriasis/cycloplegia or reverse bradycardia. Atropine may reduce gastric acid secretion in response to vagal stimulation by blocking parietal cell M3 receptors; however, it would not significantly decrease acid secretion during histamine or gastrin infusion.

**(Choice B)** Bethanechol is a cholinomimetic muscarinic agonist used to treat ileus and urinary retention. Bethanechol would promote gastric acid secretion by stimulating parietal cell M3 receptors.

**(Choice C)** Cimetidine treats gastroesophageal reflux and peptic ulcer disease by blocking parietal cell H2 receptors. Although H2 receptor blockade would reduce gastric acid secretion in response to histamine or gastrin infusion, it would not significantly reduce acid secretion in response to vagal stimulation.

**(Choice E)** Sucralfate may promote peptic ulcer healing by binding to the base of mucosal ulcers and providing physical protection against gastric acid; however, it does not inhibit gastric acid secretion.

### Educational objective:

Proton pump inhibitors (eg, omeprazole, lansoprazole) block the final common pathway of gastric acid secretion from parietal cells, which is stimulated by acetylcholine, histamine, and gastrin.

### References





A 35-year-old woman comes to the office with malaise and generalized weakness. Her other medical problems include type 1 diabetes mellitus and hypothyroidism for which she takes insulin and levothyroxine. She eats a balanced, diabetic diet and exercises 5 times per week. Physical examination shows mild conjunctival pallor.

Laboratory results are as follows:

Hemoglobin	10 g/dL
Hematocrit	30%
Mean corpuscular volume	118 fL

Further evaluation shows a very low vitamin B<sub>12</sub> level and a normal folate level. Which of the following sets of physiologic alterations is most likely to be present in this patient?

- ☐ A. Elevated gastrin, high gastric pH, and decreased parietal cell mass
- ☐ B. Elevated gastrin, high gastric pH, and increased parietal cell mass
- ☐ C. Elevated gastrin, low gastric pH, and increased parietal cell mass







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- ☐ B. Elevated gastrin, high gastric pH, and increased parietal cell mass
- ☐ C. Elevated gastrin, low gastric pH, and increased parietal cell mass
- ☐ D. Low gastrin, high gastric pH, and increased parietal cell mass
- ☐ E. Low gastrin, low gastric pH, and decreased parietal cell mass

Submit





Laboratory results are as follows.

Hemoglobin 10 g/dL

Hematocrit 30%

Mean corpuscular volume 118 fL

Further evaluation shows a very low vitamin B<sub>12</sub> level and a normal folate level. Which of the following sets of physiologic alterations is most likely to be present in this patient?

- ☒ A. Elevated gastrin, high gastric pH, and decreased parietal cell mass (55%)
- ☐ B. Elevated gastrin, high gastric pH, and increased parietal cell mass (4%)
- ☐ C. Elevated gastrin, low gastric pH, and increased parietal cell mass (14%)
- ☐ D. Low gastrin, high gastric pH, and increased parietal cell mass (5%)
- ☐ E. Low gastrin, low gastric pH, and decreased parietal cell mass (19%)

Correct



55%

Answered correctly



54 secs

Time spent



01/12/2021

Last updated

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Feedback



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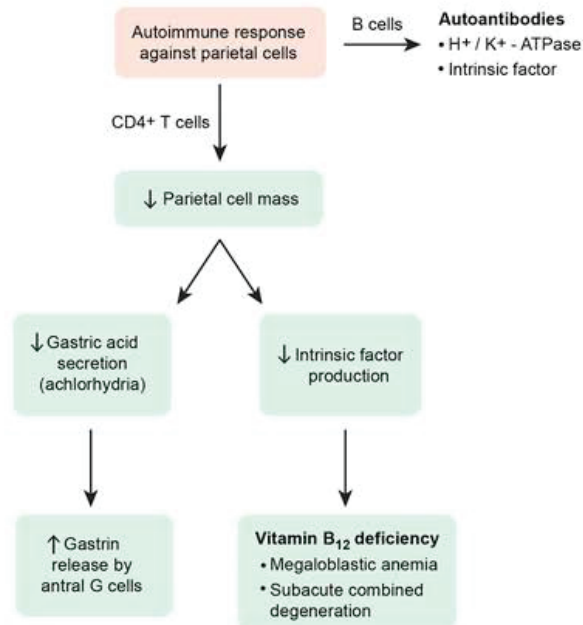


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## Exhibit Display

## Pathogenesis of autoimmune gastritis



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Zoom In

Zoom Out

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This patient's **vitamin B<sub>12</sub> (cobalamin) deficiency** in the setting of **preexisting autoimmune disease** (eg, type 1 diabetes mellitus, Hashimoto thyroiditis) is suggestive of **pernicious anemia**. This condition occurs as a result of a CD4+ cell-mediated immune response against parietal cells found in the body and fundus of the stomach (autoantibodies against parietal cell components are also produced and are useful for diagnosis but not significantly involved in the pathogenesis). Progressive destruction of oxyntic (acid-producing) mucosa leads to **loss of parietal cell mass**, causing the following effects:

- Decreased **intrinsic factor** secretion impairs absorption of dietary vitamin B<sub>12</sub> by the terminal ileum, resulting in vitamin B<sub>12</sub> deficiency and the development of **megaloblastic anemia**.
- Decreased secretion of hydrochloric acid (achlorhydria) causes an **elevated intraluminal pH** that **stimulates gastrin secretion** by gastric G cells.

**(Choice B)** Proton pump inhibitors result in elevated intraluminal pH, causing upregulation of gastrin secretion. Prolonged use may result in secondary hypertrophy and hyperplasia of parietal cells.

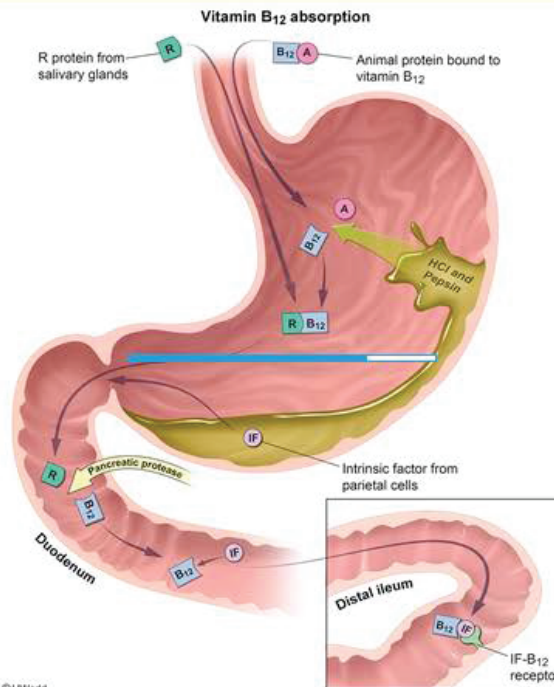
**(Choice C)** Gastrinomas are gastrin-secreting tumors commonly located in the pancreas and duodenum. Excess gastrin production leads to parietal cell hypertrophy and hydrochloric acid hypersecretion.

**(Choices D and E)** In patients with pernicious anemia, autoimmune destruction of parietal cells results in





## Exhibit Display



Zoom In

Zoom Out

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(Choices D and E) In patients with pernicious anemia, autoimmune destruction of parietal cells results in

Block Time Remaining: 00:11:55

TUTOR

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1



Feedback



Suspend



End Block



**(Choice C)** Gastrinomas are gastrin-secreting tumors commonly located in the pancreas and duodenum.

Excess gastrin production leads to parietal cell hypertrophy and hydrochloric acid hypersecretion.

**(Choices D and E)** In patients with pernicious anemia, autoimmune destruction of parietal cells results in excess gastrin production (not decreased production). This increases the risk of neuroendocrine (carcinoid) tumors.

### Educational objective:

Pernicious anemia is an autoimmune disease characterized by CD4+ cell-mediated destruction of parietal cells. As parietal cells are destroyed, their ability to secrete hydrochloric acid decreases, resulting in an elevated intraluminal pH that leads to upregulation of gastrin secretion. Patients also develop vitamin B<sub>12</sub> deficiency as a result of decreased intrinsic factor secretion.

### References

- [Diagnosis and management of pernicious anemia.](#)

Pathophysiology

Subject

Gastrointestinal & Nutrition

System

Vitamin b12 deficiency

Topic

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A 33-year-old man with a 2-year history of Crohn ileocolitis comes to the clinic with left-sided flank pain that started in the morning. The pain is 8 on a scale of 0-10 in intensity and is characterized as sharp. The pain is also colicky and radiates to the left groin. The patient has no nausea or vomiting. He is in moderate distress and has trouble lying still during the examination. Urinalysis shows hematuria. A day later, the patient passes a urinary stone. Abdominal imaging reveals several additional kidney stones. Which of the following is the most likely underlying cause of this patient's kidney stones?

- ☐ A. Defective amino acid transport
- ☐ B. Increased bone resorption
- ☐ C. Rapid cell turnover
- ☐ D. Reduced intestinal calcium oxalate formation
- ☐ E. Urinary tract infection

**Submit**



A 33-year-old man with a 2-year history of Crohn ileocolitis comes to the clinic with left-sided flank pain that started in the morning. The pain is 8 on a scale of 0-10 in intensity and is characterized as sharp. The pain is also colicky and radiates to the left groin. The patient has no nausea or vomiting. He is in moderate distress and has trouble lying still during the examination. Urinalysis shows hematuria. A day later, the patient passes a urinary stone. Abdominal imaging reveals several additional kidney stones. Which of the following is the most likely underlying cause of this patient's kidney stones?

- ☐ A. Defective amino acid transport (8%)
- ☐ B. Increased bone resorption (8%)
- ☐ C. Rapid cell turnover (7%)
- ☒ D. Reduced intestinal calcium oxalate formation (72%)
- ☐ E. Urinary tract infection (2%)

Correct



72%

Answered correctly



19 secs

Time Spent



01/06/2021

Last Updated

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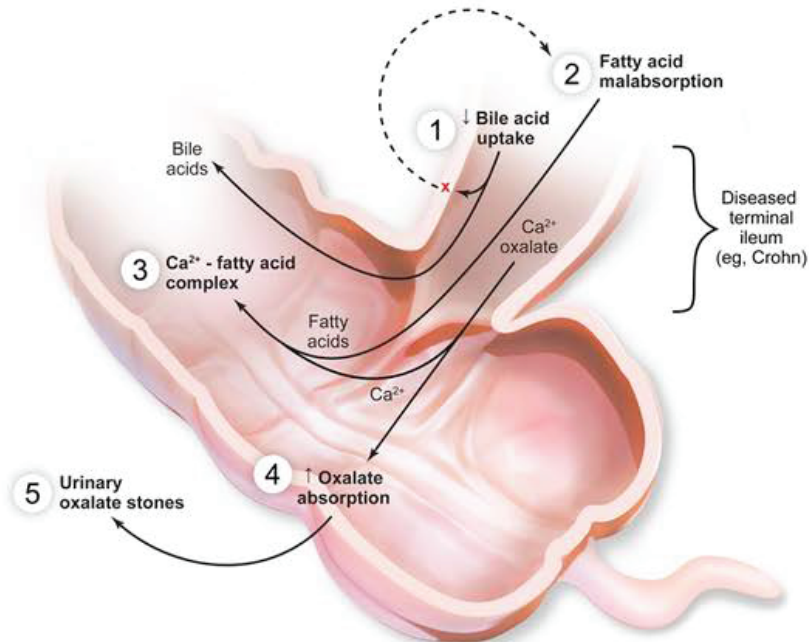


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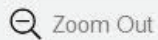
## Enteric oxaluria



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Zoom In



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Reset



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My Notebook



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Feedback



Suspend



End Block





**Crohn disease** is an inflammatory bowel disease characterized by patchy granulomatous inflammation.

Any area of the gastrointestinal tract may be involved, but involvement of the **terminal ileum** is especially common. Bile acids, which facilitate the absorption of fats and fat-soluble vitamins, are normally reabsorbed in the ileum, recycled in the liver, and then reused in the absorptive process. When the terminal ileum is inflamed, bile acids are lost in the feces, leading to **impaired fat absorption**.

In the healthy bowel, dietary calcium binds to dietary oxalate, producing insoluble calcium oxalate salts that are eliminated in the feces. But in malabsorptive syndromes such as Crohn disease, calcium forms soap complexes with the excess fat in the intestinal lumen and is unavailable for complexing with oxalate. As a result, free **oxalate absorption** is increased and subsequently filtered into the urine, promoting the formation of **oxalate kidney stones** (enteric oxaluria).

**(Choice A)** Cystinuria is an autosomal recessive condition characterized by defective dibasic amino acid transport in the proximal renal tubules. The urine becomes supersaturated with cystine, leading to formation of cystine stones beginning in childhood or adolescence. Crohn disease can cause malabsorption of dietary protein and amino acids, but this is due to inflammation, not abnormal amino acid transporters; patients are not predisposed to cystine stones.

**(Choice B)** Patients with Crohn disease commonly develop vitamin/nutrient deficiencies (eg, vitamin D,





transporters; patients are not predisposed to cystine stones.

**(Choice B)** Patients with Crohn disease commonly develop vitamin/nutrient deficiencies (eg, vitamin D, calcium) due to malabsorption, which can reduce bone mineral density and increase the risk of fractures. Secondary hyperparathyroidism may be present, but unlike primary hyperparathyroidism does not promote kidney stone formation.

**(Choice C)** Uric acid stones may develop from conditions associated with rapid cell turnover (eg, myeloproliferative disease, hemolytic anemia) due to chronically increased uric acid production. The stones seen in Crohn disease are composed of calcium oxalate rather than uric acid.

**(Choice E)** Alkalinization of the urine by urease-producing organisms (eg, *Proteus*, *Klebsiella*) in the upper urinary tract can promote formation of stones made up of magnesium ammonium phosphate (struvite) and calcium carbonate apatite. Although patients with Crohn disease can develop enterovesicular fistulas and recurrent urinary tract infections, this patient has no features of urinary infection (eg, fever, dysuria, pyuria).

**Educational objective:**

Crohn disease is associated with oxalate kidney stones. Impaired bile acid absorption in the terminal ileum leads to loss of bile acids in feces with subsequent fat malabsorption. Intestinal lipids then bind calcium ions, and the resulting soap complex is excreted. Free oxalate (normally bound by calcium to form an





Secondary hyperparathyroidism may be present, but unlike primary hyperparathyroidism does not promote kidney stone formation.

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### Educational objective:

Crohn disease is associated with oxalate kidney stones. Impaired bile acid absorption in the terminal ileum leads to loss of bile acids in feces with subsequent fat malabsorption. Intestinal lipids then bind calcium ions, and the resulting soap complex is excreted. Free oxalate (normally bound by calcium to form an unabsorbable complex) is absorbed and forms urinary calculi (enteric oxaluria).

### References

- [Urolithiasis in inflammatory bowel disease and bariatric surgery.](#)





A 3-day-old boy is brought to the emergency department due to poor feeding, emesis, and lethargy over the last 24 hours. The patient was born via uncomplicated spontaneous vaginal delivery to a 30-year-old woman who had a normal pregnancy. The boy was discharged from the newborn nursery yesterday and was breastfeeding exclusively until the onset of symptoms. Stool and urine output were normal while he was in the newborn nursery. The patient is afebrile and normotensive but tachycardic and tachypneic. He appears dehydrated, and the abdomen is distended. The patient vomits during the examination, and the vomitus is shown in the [exhibit](#). On laparotomy, fibrous bands are seen extending from the cecum and right colon to the retroperitoneum, causing extrinsic compression of the duodenum. Which of the following embryologic processes most likely failed in this patient?

- ☐ A. Failure of gut recanalization
- ☒ B. Fusion of the ventral and dorsal pancreatic buds
- ☐ C. Midgut rotation around the superior mesenteric artery
- ☐ D. Neural crest cell migration into the bowel wall
- ☐ E. Obliteration of the omphalomesenteric duct





Item 17 of 40

Question Id: 318



Mark



Previous



Next



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Lab Values



Notes



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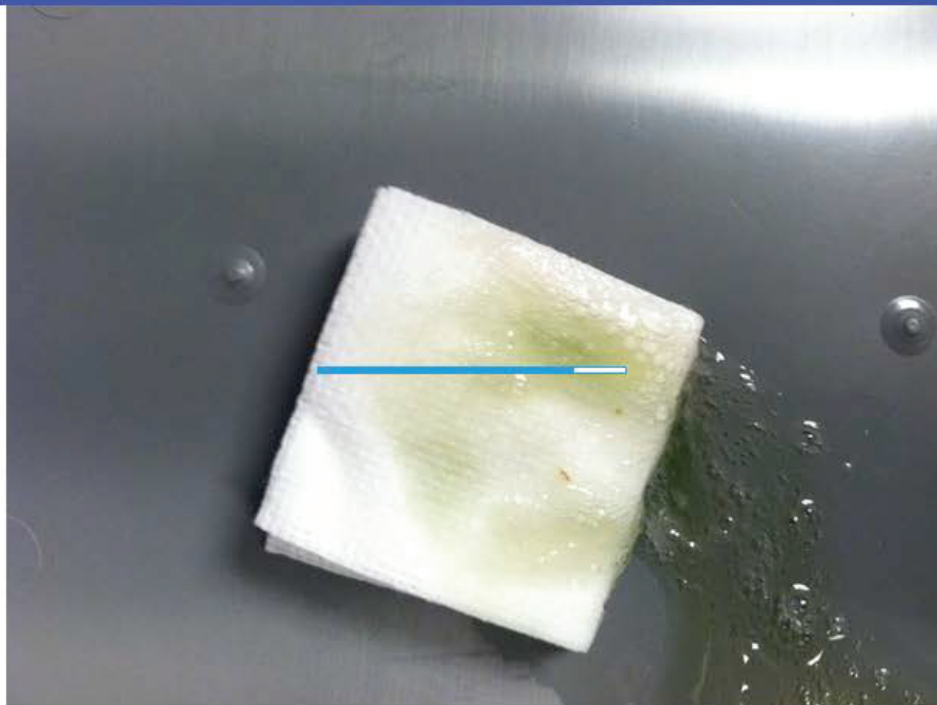


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the last 24 hours. The patient was born via uncomplicated spontaneous vaginal delivery to a 30-year-old woman who had a normal pregnancy. The boy was discharged from the newborn nursery yesterday and was breastfeeding exclusively until the onset of symptoms. Stool and urine output were normal while he was in the newborn nursery. The patient is afebrile and normotensive but tachycardic and tachypneic. He appears dehydrated, and the abdomen is distended. The patient vomits during the examination, and the vomitus is shown in the [exhibit](#). On laparotomy, fibrous bands are seen extending from the cecum and right colon to the retroperitoneum, causing extrinsic compression of the duodenum. Which of the following embryologic processes most likely failed in this patient?

- ☐ A. Failure of gut recanalization (14%)
- ☐ B. Fusion of the ventral and dorsal pancreatic buds (9%)
- ☒ C. Midgut rotation around the superior mesenteric artery (53%)
- ☐ D. Neural crest cell migration into the bowel wall (4%)
- ☐ E. Obliteration of the omphalomesenteric duct (17%)





Around 6 weeks gestation, the midgut (supplied by the superior mesenteric artery) herniates through the umbilical ring in order to grow rapidly. During this process, the midgut rotates 90 degrees counterclockwise. Following additional growth, the midgut returns to the abdominal cavity at 8-10 weeks gestation and turns an additional 180 degrees counterclockwise (270 degrees total). Subsequently, the gut is fixed to the posterior abdomen on a wide-based mesentery.

Incomplete counterclockwise rotation (eg, 180 degrees) will result in **midgut malrotation**. The cecum will rest in the right upper quadrant instead of the right lower quadrant (RLQ). Additionally, **Ladd's (fibrous) bands** connect the retroperitoneum in the RLQ to the right colon/cecum by passing over the second part of the duodenum, causing **intestinal obstruction** in the process. Obstruction manifests as bilious emesis during the first days of life. In addition, because the mesenteric base is abnormally narrowed, the mesentery is vulnerable to twisting around the **superior mesenteric artery**. The twisting, referred to as midgut **volvulus**, compromises intestinal perfusion and may lead to life-threatening bowel necrosis.

**(Choice A)** Failure of gut recanalization is a possible mechanism for development of **duodenal atresia** (distension of stomach and duodenum on X-ray). Ladd's bands are not found in this condition.

**(Choice B)** Failure of ventral and dorsal pancreatic buds to fuse at 8 weeks gestation results in pancreas





Item 17 of 40

Question Id: 318



Mark



Previous



Next



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Notes



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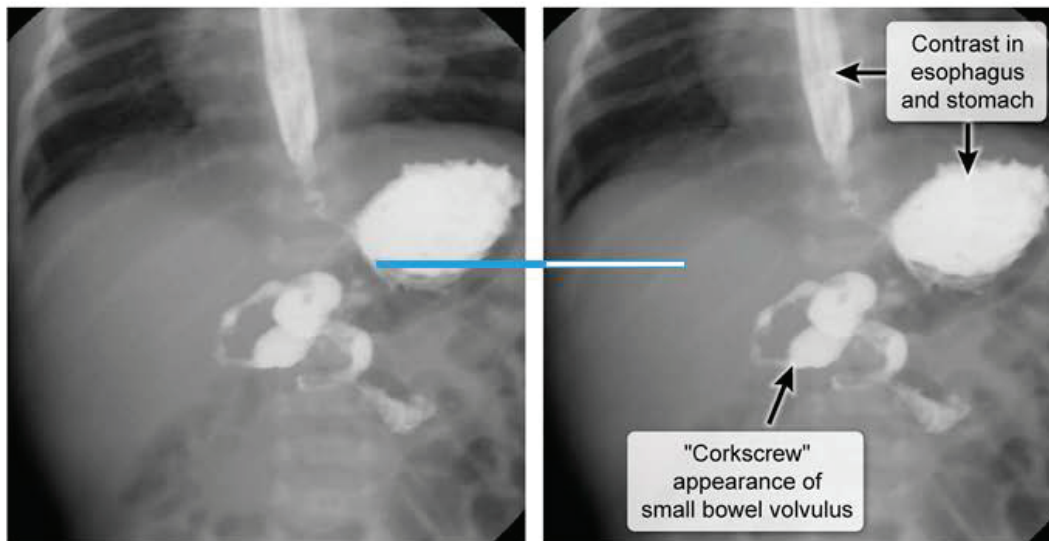
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## Midgut volvulus



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Item 17 of 40

Question Id: 318



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

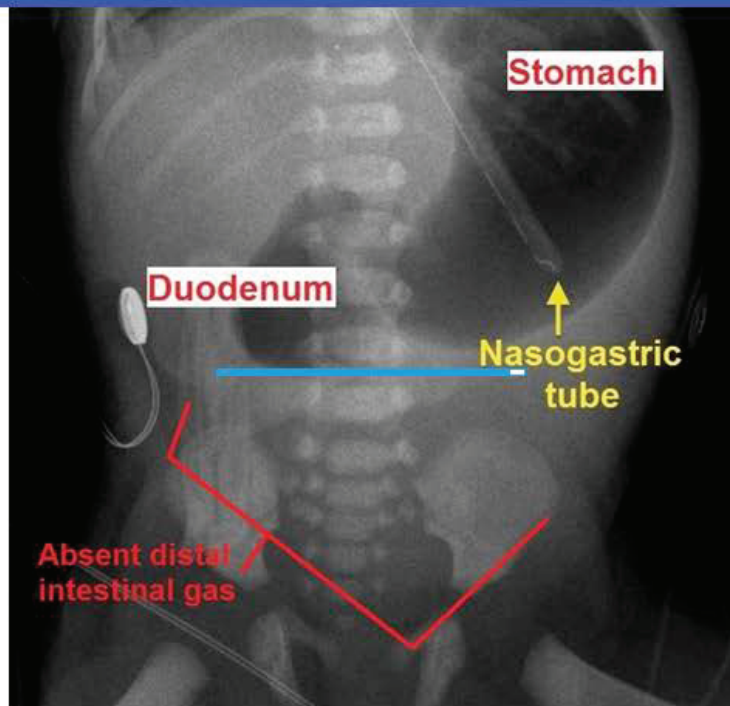
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### Exhibit Display



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(distension of stomach and duodenum on X-ray). Ladd's bands are not found in this condition.

**(Choice B)** Failure of ventral and dorsal pancreatic buds to fuse at 8 weeks gestation results in pancreas divisum. However, this condition is usually asymptomatic and an incidental finding on imaging study or autopsy.

**(Choice D)** Failure of neural crest cell migration in the gut causes aganglionic sigmoid colon/rectum. The affected bowel segments cannot relax and are therefore narrow and obstructive. [Hirschsprung disease](#) presents in the neonatal period with delayed passage of meconium, abdominal distension, and bilious emesis.

**(Choice E)** The omphalomesenteric duct connects the midgut lumen with the yolk sac. Failed obliteration of the duct causes vitelline fistula (complete failure) or a [Meckel diverticulum](#) (partial failure). If symptomatic, Meckel diverticulum most commonly presents with painless lower gastrointestinal bleeding without emesis.

**Educational objective:**

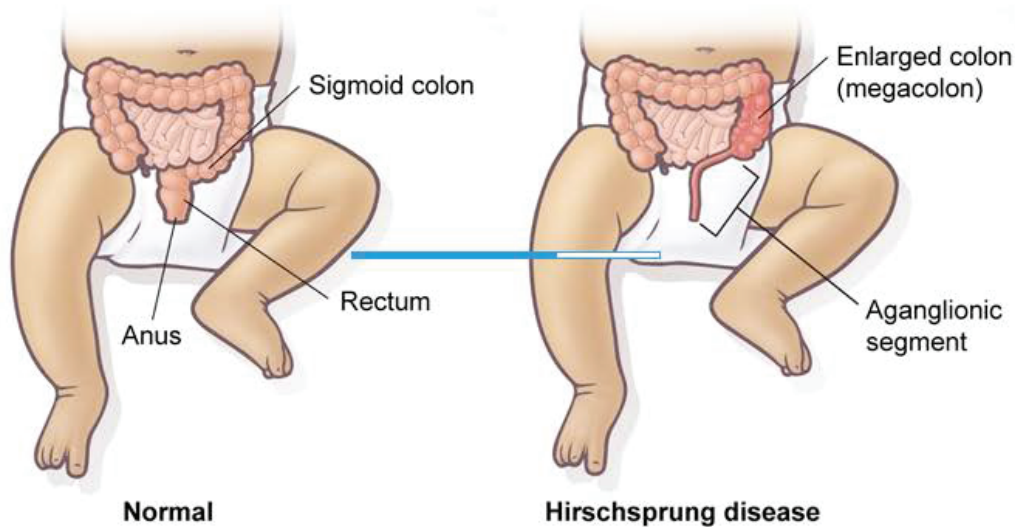
Intestinal malrotation results when the midgut undergoes incomplete embryological counterclockwise rotation. It can present as intestinal obstruction (due to compression by the adhesive bands) and midgut volvulus (intestinal ischemia due to twisting around the blood vessels).





## Exhibit Display

## Hirschsprung disease



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Item 17 of 40

Question Id: 318



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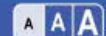
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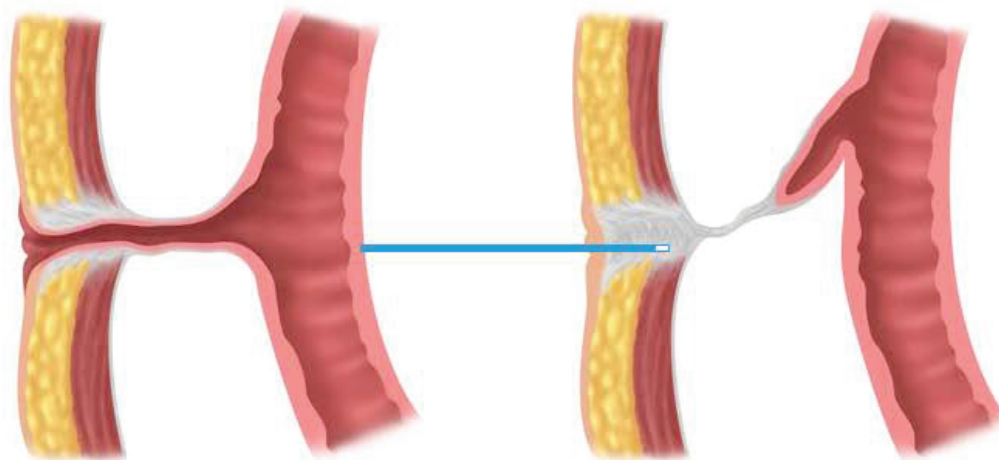
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## Exhibit Display

## Vitelline duct abnormalities



Persistent vitelline duct

Meckel diverticulum

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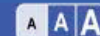


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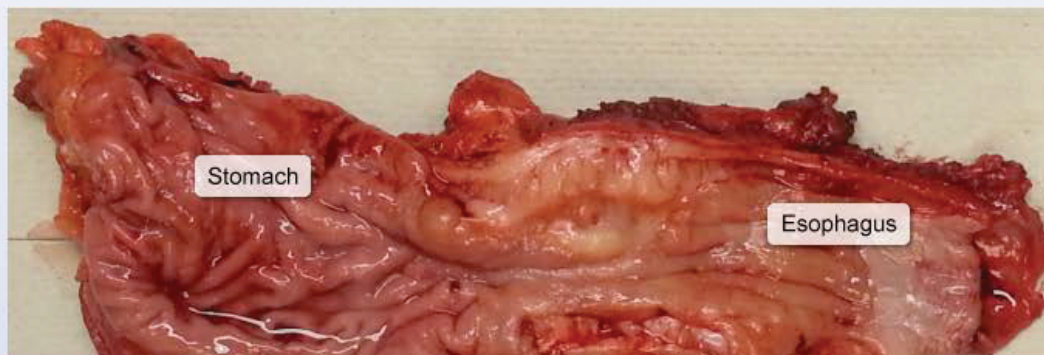


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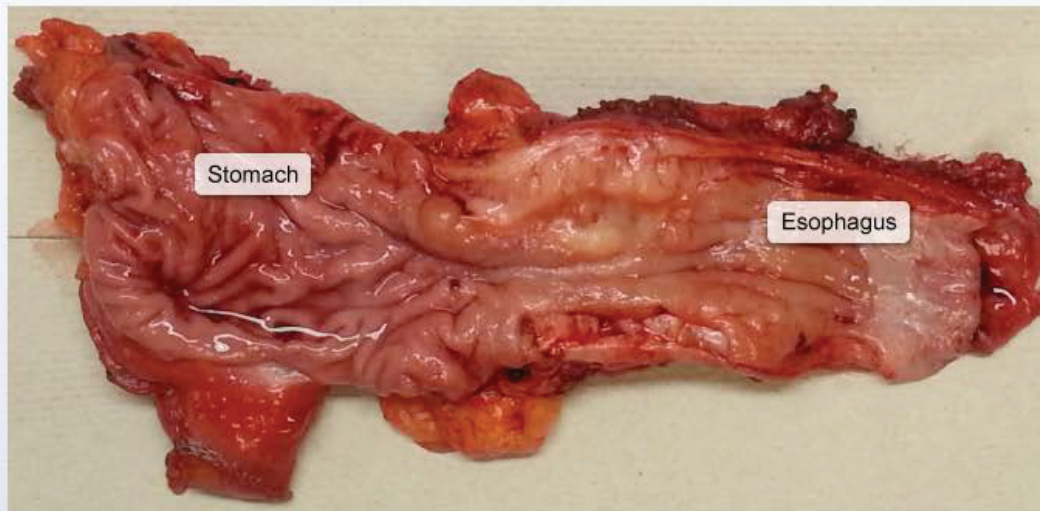




A 65-year-old man with a history of chronic gastroesophageal reflux comes to the clinic due to dysphagia. The patient has had difficulty swallowing foods such as steak or hard-boiled eggs but is able to drink hot tea and coffee without any issues. Increasing the frequency of his proton pump inhibitor to twice daily did not improve symptoms. He has also lost 6.8 kg (15 lb) over the past 4 months. The patient has a history of hypertension, hyperlipidemia, and osteoarthritis. Medications include amlodipine, atorvastatin, and ibuprofen as needed. He drinks 2 or 3 glasses of wine with dinner most nights but does not use tobacco or illicit drugs. Vital signs are within normal limits. BMI is 32 kg/m<sup>2</sup>. Physical examination is unremarkable. Esophagogastroduodenoscopy reveals a 4-cm mass surrounded by a large segment of discolored mucosa in the lower half of the esophagus. Esophagogastrrectomy results are shown in the image below:

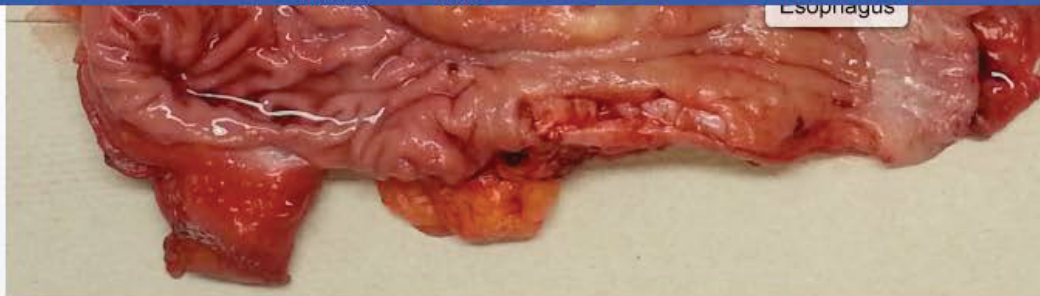


lisinopril as needed. He drinks 2 or 3 glasses of wine with dinner most nights but does not use tobacco or illicit drugs. Vital signs are within normal limits. BMI is 32 kg/m<sup>2</sup>. Physical examination is unremarkable. Esophagogastroduodenoscopy reveals a 4-cm mass surrounded by a large segment of discolored mucosa in the lower half of the esophagus. Esophagogastrectomy results are shown in the image below:



Which of the following is the most likely predisposing factor for this patient's esophageal disease?

☐ A. Alcohol use

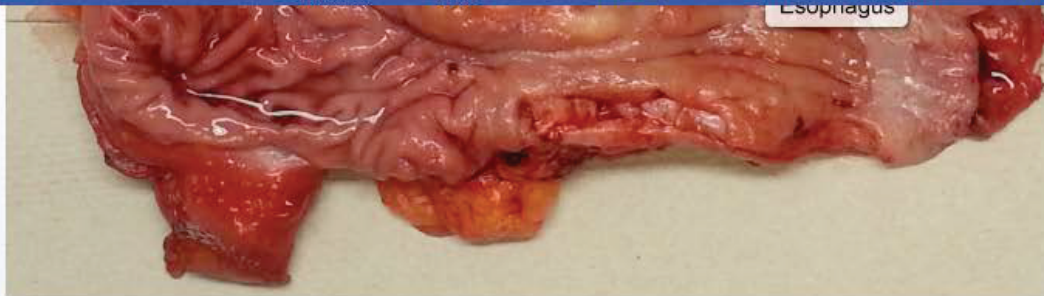


Which of the following is the most likely predisposing factor for this patient's esophageal disease?

- ☐ A. Alcohol use
- ☐ B. Chronic nonsteroidal anti-inflammatory drug use
- ☐ C. *Helicobacter pylori* infection
- ☐ D. Obesity
- ☐ E. Repeated thermal injury

Submit





Which of the following is the most likely predisposing factor for this patient's esophageal disease?

- ☐ A. Alcohol use (24%)
- ☐ B. Chronic nonsteroidal anti-inflammatory drug use (8%)
- ☐ C. *Helicobacter pylori* infection (16%)
- ☒ D. Obesity (39%)
- ☐ E. Repeated thermal injury (11%)

Correct

39%

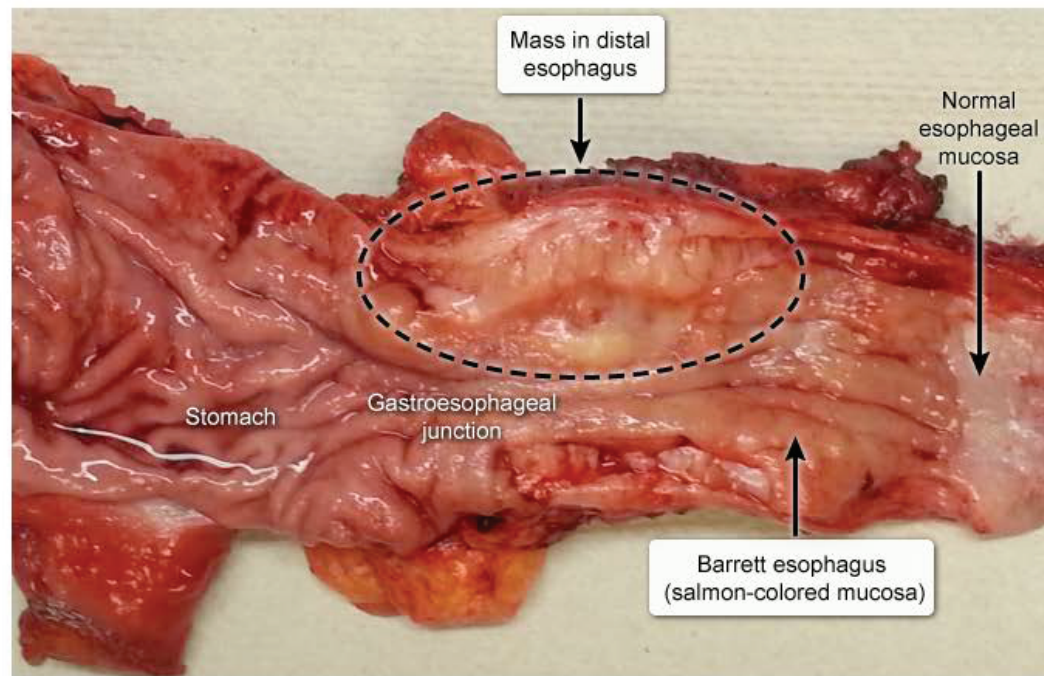
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01/24/2021





## Esophageal adenocarcinoma



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This patient with chronic gastroesophageal reflux disease (GERD) now has dysphagia with solid foods.

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This patient with chronic gastroesophageal reflux disease (GERD) now has dysphagia with solid foods, weight loss, and a mass in his lower esophagus, raising strong suspicion for **esophageal adenocarcinoma**. Most cases of esophageal adenocarcinoma arise in the setting of **Barrett esophagus**, a metaplastic condition whereby the normal stratified squamous epithelium in the distal esophagus is **replaced** with intestine-like columnar cells in response to chronic acidic damage. Although these metaplastic columnar cells are better suited to handle the presence of acid in the distal esophagus, they are also much more likely to become dysplastic and undergo malignant transformation into esophageal adenocarcinoma.

Major risk factors for esophageal adenocarcinoma are similar to those that promote Barrett esophagus and include:

- **Chronic GERD**
- **Obesity** - increases intragastric pressure, frequency of lower esophageal sphincter relaxation, and rates of hiatal hernia, which promote GERD
- Smoking
- Use of medications that lower esophageal sphincter pressure (eg, nitroglycerin)

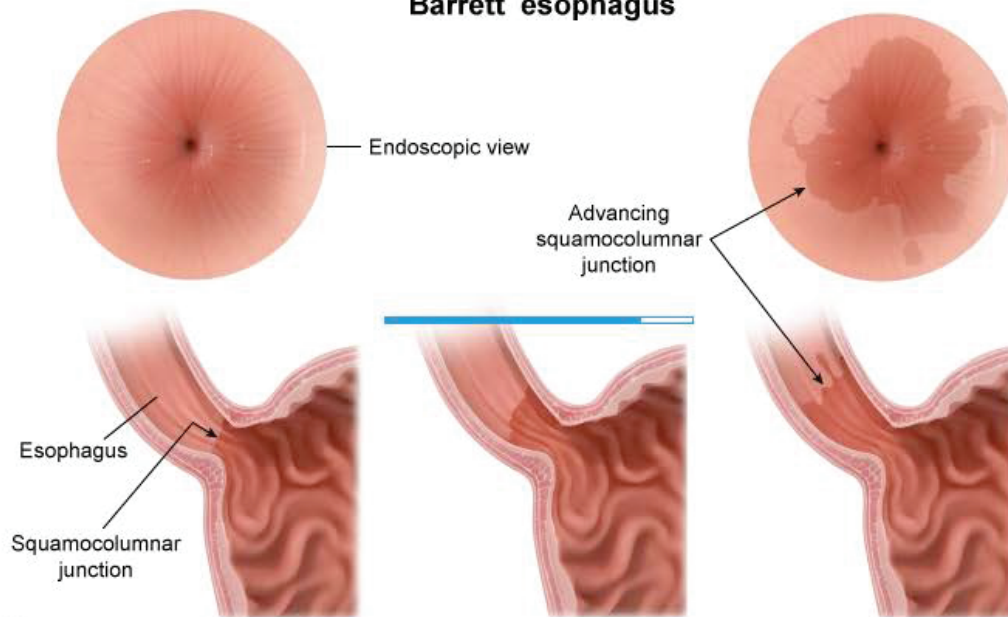




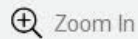


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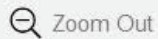
## Barrett esophagus



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- Smoking
- Use of medications that lower esophageal sphincter pressure (eg, nitroglycerin)
- Consumption of foods containing nitroso compounds (eg, processed meats)

**(Choice A)** Alcohol is a risk factor for esophageal squamous cell carcinoma, which typically arises in the mid-esophagus from areas of esophageal squamous dysplasia. Alcohol does not appear to increase the risk of Barrett esophagus, and wine may be protective.

**(Choice B)** Aspirin and other nonsteroidal anti-inflammatory drugs may be protective against esophageal cancer, especially in the setting of Barrett esophagus. These drugs may also be protective against colorectal cancer.

**(Choice C)** *Helicobacter pylori* is an important risk factor for gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue; it does not appear to increase risk for esophageal adenocarcinoma.

**(Choice E)** Thermal injury due to drinking hot beverages may increase the risk of esophageal squamous cell carcinoma but is not clearly associated with esophageal adenocarcinoma.

**Educational objective:**

Esophageal adenocarcinoma usually occurs in the distal esophagus due to underlying Barrett esophagus.





risk of Barrett esophagus, and wine may be protective.

**(Choice B)** Aspirin and other nonsteroidal anti-inflammatory drugs may be protective against esophageal cancer, especially in the setting of Barrett esophagus. These drugs may also be protective against colorectal cancer.

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**(Choice E)** Thermal injury due to drinking hot beverages may increase the risk of esophageal squamous cell carcinoma but is not clearly associated with esophageal adenocarcinoma.

### Educational objective:

Esophageal adenocarcinoma usually occurs in the distal esophagus due to underlying Barrett esophagus. Long-standing gastroesophageal reflux disease is the most important risk factor. Obesity, smoking, use of medications that lower esophageal sphincter pressure, and consumption of foods containing nitroso compounds also increase the risk.

### References

- Epidemiology, diagnosis, and management of esophageal adenocarcinoma.
- Etiology and prevention of esophageal cancer.



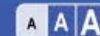




A 52-year-old woman comes to the office with a 2-month history of skin rash that worsens with sun exposure. Her family says that lately she has become irritable, hostile, and has had episodes of disorientation. The patient does not use tobacco or illicit drugs but has been drinking half a bottle of gin daily. Further questioning reveals poor nutritional intake and intermittent diarrhea. The patient restricts her diet for weight control. Body mass index is 17 kg/m<sup>2</sup>. On examination, she has a well-demarcated, hyperpigmented, scaly rash on the hands, forearms, and upper chest. The cause of most of her symptoms is determined to be a lack of the precursor vitamin for synthesis of NAD<sup>+</sup> coenzyme. The compensatory pathway to synthesize this coenzyme uses which of the following as a precursor?

- ☐ A. Arginine
- ☐ B. Carotene
- ☐ C. Cholesterol
- ☐ D. Orotic acid
- ☐ E. Phenylalanine
- ☐ F. Tryptophan

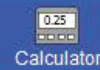
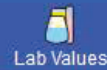




exposure. Her family says that lately she has become irritable, hostile, and has had episodes of disorientation. The patient does not use tobacco or illicit drugs but has been drinking half a bottle of gin daily. Further questioning reveals poor nutritional intake and intermittent diarrhea. The patient restricts her diet for weight control. Body mass index is  $17 \text{ kg/m}^2$ . On examination, she has a well-demarcated, hyperpigmented, scaly rash on the hands, forearms, and upper chest. The cause of most of her symptoms is determined to be a lack of the precursor vitamin for synthesis of  $\text{NAD}^+$  coenzyme. The compensatory pathway to synthesize this coenzyme uses which of the following as a precursor?

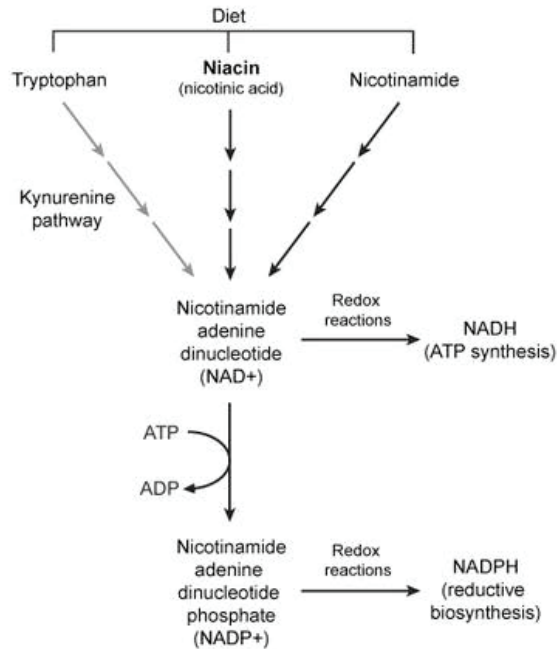
- ☐ A. Arginine (15%)
- ☐ B. Carotene (5%)
- ☐ C. Cholesterol (3%)
- ☐ D. Orotic acid (7%)
- ☐ E. Phenylalanine (7%)
- ☒ F. Tryptophan (60%)



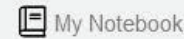
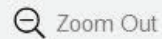
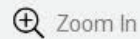


## Exhibit Display

## Niacin metabolism



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**Pellagra** ("rough skin" in Italian vernacular) is due to **niacin deficiency** and is characterized by the "3 Ds": **dermatitis, diarrhea, and dementia**:

- **Dermatitis** is bilateral and symmetric on sun-exposed areas of the body and is characterized by rough, thick, scaly skin.
- Diarrhea is due to atrophy (and occasional ulceration) of columnar epithelium of the gastrointestinal tract.
- Dementia is due to neuronal degeneration in the brain and spinal cord, with lesions similar to those associated with pernicious anemia.

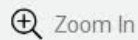
Niacin (nicotinic acid, or vitamin B<sub>3</sub>) is an essential component of the coenzymes nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), which participate in redox metabolism. Specifically, NAD functions as a coenzyme for dehydrogenases involved in the metabolism of fats, carbohydrates, and amino acids; NADP is crucial in the hexose-monophosphate shunt of glucose metabolism and for biosynthesis of cholesterol and fatty acids.

Niacin can be obtained through dietary intake or **synthesized endogenously** from **tryptophan**. In developing countries, niacin deficiency is seen in populations that subsist primarily on corn products (niacin in corn occurs in a bound, unabsorbable form). In developed countries, it is primarily seen in patients with

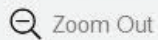




Exhibit Display



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Niacin can be obtained through dietary intake or **synthesized endogenously** from **tryptophan**. In developing countries, niacin deficiency is seen in populations that subsist primarily on corn products (niacin in corn occurs in a bound, unabsorbable form). In developed countries, it is primarily seen in patients with impaired nutritional intake (eg, alcoholism, chronic illness). Pellagra can also be seen occasionally in those with carcinoid syndrome, prolonged isoniazid therapy, or Hartnup disease.

**(Choice A)** Arginine is the precursor of nitric oxide, urea, ornithine, and agmatine. It is also necessary for the formation of creatine.

**(Choice B)** Carotene is the precursor to vitamin A.

**(Choice C)** Cholesterol is the precursor to steroid hormones.

**(Choice D)** Orotic acid is a precursor of pyrimidine.

**(Choice E)** Phenylalanine is the precursor to tyrosine, an amino acid necessary for the formation of catecholamines.

**Educational objective:**

Niacin (vitamin B<sub>3</sub>) can be synthesized endogenously from tryptophan and is an essential component of nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). A







with carcinoid syndrome, prolonged isoniazid therapy, or Hartnup disease.

**(Choice A)** Arginine is the precursor of nitric oxide, urea, ornithine, and agmatine. It is also necessary for the formation of creatine.

**(Choice B)** Carotene is the precursor to vitamin A.

**(Choice C)** Cholesterol is the precursor to steroid hormones.

**(Choice D)** Orotic acid is a precursor of pyrimidine.

**(Choice E)** Phenylalanine is the precursor to tyrosine, an amino acid necessary for the formation of catecholamines.

### Educational objective:

Niacin (vitamin B<sub>3</sub>) can be synthesized endogenously from tryptophan and is an essential component of nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). A deficiency of this vitamin results in pellagra, which is characterized by dermatitis, diarrhea, and dementia.

### References

- [Pellagra and alcoholism: a biochemical perspective.](#)





A 16-year-old boy is brought to the office by his parents due to tremors and difficulty walking. Over the past year, his school performance has declined, and he has been moodier and more impulsive. His parents also note that he has been sleeping more than usual and has had a poor appetite for the past 2 months. Approximately 3 weeks ago, the patient developed a tremor in both hands that is most prominent when he reaches for an object or tries to write. The tremor has worsened significantly over the past week, and he has developed an unsteady, broad-based gait. Laboratory studies reveal elevated serum transaminases and 24-hour urinary copper excretion. The patient is prescribed penicillamine therapy. This medication primarily works through which of the following mechanisms?

- ☐ A. Decreasing intestinal absorption of copper
- ☐ B. Increasing urinary excretion of copper
- ☐ C. Repletion of intracellular glutathione
- ☐ D. Stimulation of defective gene expression
- ☐ E. Stimulation of canalicular transport proteins





year, his school performance has declined, and he has been moodier and more impulsive. His parents also note that he has been sleeping more than usual and has had a poor appetite for the past 2 months. Approximately 3 weeks ago, the patient developed a tremor in both hands that is most prominent when he reaches for an object or tries to write. The tremor has worsened significantly over the past week, and he has developed an unsteady, broad-based gait. Laboratory studies reveal elevated serum transaminases and 24-hour urinary copper excretion. The patient is prescribed penicillamine therapy. This medication primarily works through which of the following mechanisms?

- ☐ A. Decreasing intestinal absorption of copper (37%)
- ☒ B. Increasing urinary excretion of copper (56%)
- ☐ C. Repletion of intracellular glutathione (1%)
- ☐ D. Stimulation of defective gene expression (0%)
- ☐ E. Stimulation of canalicular transport proteins (3%)

Correct



56%

Answered correctly



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### Wilson disease

#### Pathogenesis

- Autosomal recessive mutation of *ATP7B* → hepatic copper accumulation → leak from damaged hepatocytes → deposits in tissues (eg, basal ganglia, cornea)

#### Clinical findings

- Hepatic (acute liver failure, chronic hepatitis, cirrhosis)
- Neurologic (parkinsonism, gait disturbance, dysarthria)
- Psychiatric (depression, personality changes, psychosis)

#### Diagnosis

- ↓ Ceruloplasmin & ↑ urinary copper excretion
- Kayser-Fleischer rings on slit-lamp examination



**Clinical findings**

- Hepatic (acute liver failure, chronic hepatitis, cirrhosis)
- Neurologic (parkinsonism, gait disturbance, dysarthria)
- Psychiatric (depression, personality changes, psychosis)

**Diagnosis**

- ↓ Ceruloplasmin & ↑ urinary copper excretion
- Kayser-Fleischer rings on slit-lamp examination
- ↑ Copper content on liver biopsy

**Treatment**

- Chelators (eg, D-penicillamine, trientine)
- Zinc (interferes with copper absorption)

This patient has **Wilson disease**, an autosomal recessive disorder characterized by excessive copper deposition in the liver, basal ganglia, and cornea.





This patient has **Wilson disease**, an autosomal recessive disorder characterized by excessive copper deposition in the liver, basal ganglia, and cornea.

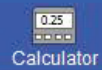
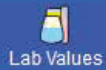
Copper is an essential nutrient that is absorbed in the intestines, metabolized by hepatocytes, and excreted in the bile. Pathogenesis of Wilson disease involves **impaired hepatocellular copper transport**, which results in **decreased biliary excretion of copper**. The resultant increase in intracellular copper causes oxidative stress and apoptosis of hepatocytes, which leads to liver dysfunction (eg, elevated transaminases, liver failure). Excess copper is then released into the bloodstream and deposited into extrahepatic tissues, causing neurologic (eg, tremor, ataxia) and psychiatric symptoms (eg, impulsivity, depressive symptoms). Although renal excretion of copper in healthy patients is extremely low, the relative increase in serum copper in Wilson disease results in increased urinary excretion of copper, as seen in this patient.

**First-line treatment** of Wilson disease is with **penicillamine**, a **copper chelating agent**. Penicillamine binds free copper as well as reduces copper bound to other proteins. This reduction preferentially increases affinity of copper to the chelating agent. The chelator-copper complex is soluble, thereby **increasing urinary copper excretion**.

**(Choice A)** Zinc decreases intestinal absorption of copper and can be used in conjunction with



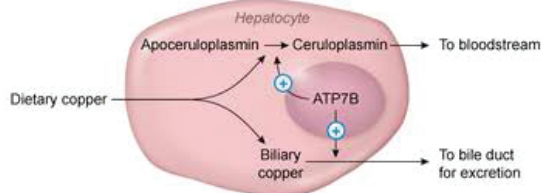




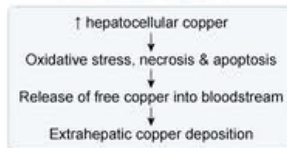
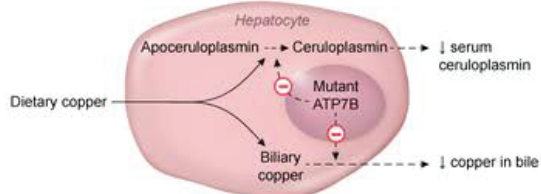
### Exhibit Display

#### Copper metabolism and Wilson disease

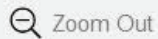
##### Normal copper metabolism



##### Impaired copper metabolism in Wilson disease



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increasing urinary copper excretion.

**(Choice A)** Zinc decreases intestinal absorption of copper and can be used in conjunction with penicillamine to treat Wilson disease.

**(Choice C)** Acetaminophen overdose causes hepatotoxicity via depletion of intracellular glutathione, which can be reversed with N-acetylcysteine treatment.

**(Choices D and E)** Gene therapy could theoretically improve or cure Wilson disease by transferring a functional copper transport protein gene into hepatocytes. This would restore their ability to transport excess copper into secretory vesicles, promoting exocytosis of copper into the bile canaliculi.

### Educational objective:

Penicillamine, a first-line treatment for Wilson disease, is a copper chelating agent that increases the urinary excretion of copper.

### References

- [Clinical management of Wilson disease.](#)

Pharmacology      Gastrointestinal & Nutrition      Wilson disease  
Subject      System      Topic

Block Time Remaining: 00:14:38

TUTOR

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Feedback

Suspend

End Block



A 71-year-old man comes to the emergency department due to several episodes of bright red blood per rectum. His recent colonoscopy revealed numerous colonic diverticula. Laboratory studies on admission are notable for a hemoglobin of 8.2 g/dL with an unremarkable coagulation profile. An abdominal angiogram shows active bleeding from the sigmoid colon. Catheter embolization is planned via the femoral artery. During the procedure, the arterial catheter is most likely to proceed in which of the following orders?

- ☐ A. External iliac, common iliac, abdominal aorta, celiac
- ☐ B. External iliac, common iliac, abdominal aorta, inferior mesenteric
- ☐ C. External iliac, common iliac, abdominal aorta, superior mesenteric
- ☐ D. External iliac, internal iliac, internal pudendal
- ☐ E. External iliac, internal iliac, middle rectal

Submit









A 71-year-old man comes to the emergency department due to several episodes of bright red blood per rectum. His recent colonoscopy revealed numerous colonic diverticula. Laboratory studies on admission are notable for a hemoglobin of 8.2 g/dL with an unremarkable coagulation profile. An abdominal angiogram shows active bleeding from the sigmoid colon. Catheter embolization is planned via the femoral artery. During the procedure, the arterial catheter is most likely to proceed in which of the following orders?

- ☐ A. External iliac, common iliac, abdominal aorta, celiac (1%)
- ☒ B. External iliac, common iliac, abdominal aorta, inferior mesenteric (86%)
- ☐ C. External iliac, common iliac, abdominal aorta, superior mesenteric (5%)
- ☐ D. External iliac, internal iliac, internal pudendal (3%)
- ☐ E. External iliac, internal iliac, middle rectal (3%)

Correct

 86%  
Answered correctly

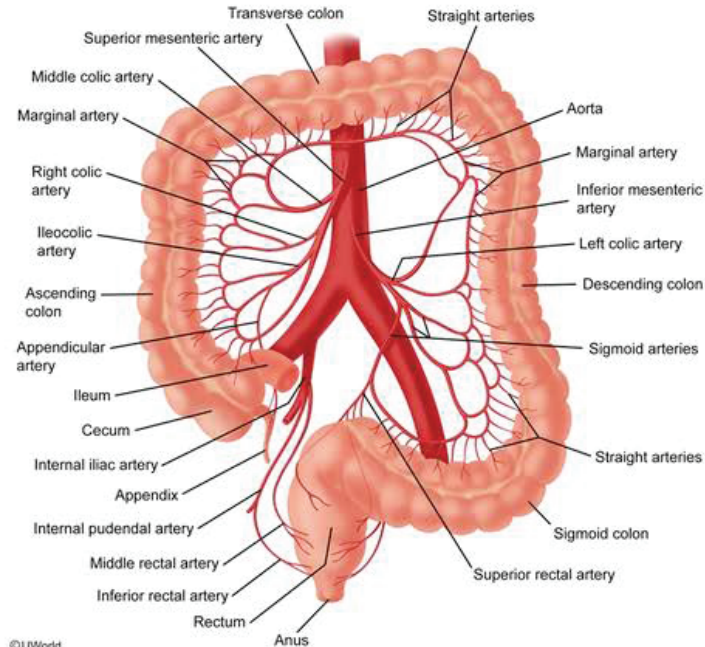
 22 secs  
Time Spent

 10/12/2020  
Last Updated



### Exhibit Display

#### Arteries of the large intestine



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Previous



Next



Full Screen



Tutorial



Lab Values



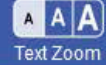
Notes



Calculator



Reverse Color



Text Zoom



Settings

In this patient with recurrent gastrointestinal bleeding, arterial embolization (mechanical occlusion of the artery using coils or absorbable substances) is planned to stop the active bleeding originating from his sigmoid colon. The distal one-third of the transverse colon, descending colon, **sigmoid** colon, and rectum are all **hindgut** derivatives. Hindgut structures receive blood from the **inferior mesenteric artery** (IMA), a branch of the aorta. These structures are drained by the inferior mesenteric vein (IMV), which does not course with the IMA. The IMV drains blood from the hindgut into the splenic vein, which drains into the portal vein.

**(Choice A)** The celiac trunk supplies blood to most foregut structures from the lower esophagus to the second part of the duodenum. Foregut derivatives include the liver, pancreas, and gallbladder. The celiac trunk also supplies the spleen.

**(Choice C)** The superior mesenteric artery supplies blood to the midgut, which spans from the third part of the duodenum to the proximal two-thirds of the transverse colon.

**(Choices D and E)** The internal iliac artery supplies portions of the gut through branches such as the inferior rectal artery (a branch of the internal pudendal artery, which arises from the internal iliac artery) and the middle rectal artery (arises from the internal iliac). The internal pudendal artery supplies blood to the external genitalia. The superior rectal artery is a continuation of the IMA.



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Feedback



Suspend



End Block



**(Choice A)** The celiac trunk supplies blood to most foregut structures from the lower esophagus to the second part of the duodenum. Foregut derivatives include the liver, pancreas, and gallbladder. The celiac trunk also supplies the spleen.

**(Choice C)** The superior mesenteric artery supplies blood to the midgut, which spans from the third part of the duodenum to the proximal two-thirds of the transverse colon.

**(Choices D and E)** The internal iliac artery supplies portions of the gut through branches such as the inferior rectal artery (a branch of the internal pudendal artery, which arises from the internal iliac artery) and the middle rectal artery (arises from the internal iliac). The internal pudendal artery supplies blood to the external genitalia. The superior rectal artery is a continuation of the IMA.

### Educational objective:

The hindgut encompasses the distal one-third of the transverse colon, the descending colon, the sigmoid colon, and the rectum. These structures receive their main arterial blood supply from the inferior mesenteric artery.

Anatomy

Gastrointestinal & Nutrition

Gastrointestinal hemorrhage

Subject

System

Topic

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Block Time Remaining: 00:15:00

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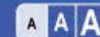
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Feedback

Suspend

End Block



A 32-year-old woman comes to the clinic due to 6 weeks of bloating and nonbloody diarrhea. She describes having multiple watery bowel movements a day without visible blood. She underwent gastric bypass surgery for morbid obesity 3 years ago. The patient has no other medical conditions. She is a lifelong nonsmoker and does not drink alcohol. Her vital signs are within normal limits. Physical examination is unremarkable. A jejunal aspirate shows bacterial count of  $>10^5$  organisms/mL, consistent with small intestinal bacterial overgrowth. Which of the following serum substance levels is most likely to be increased in this patient?

- ☐ A. Cobalamin
- ☐ B. Folate
- ☐ C. Iron
- ☐ D. Vitamin D<sub>2</sub>
- ☐ E. Zinc

**Submit**

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1



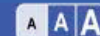
Feedback



Suspend



End Block



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- ☐ A. Cobalamin (15%)
- ☒ B. Folate (32%)
- ☐ C. Iron (18%)
- ☐ D. Vitamin D<sub>2</sub> (18%)
- ☐ E. Zinc (14%)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



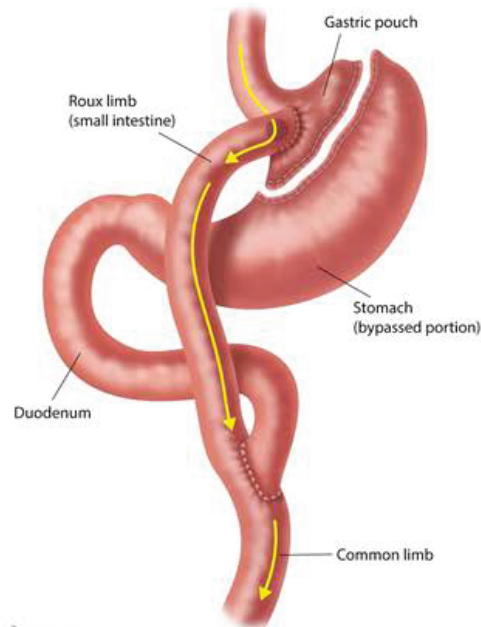
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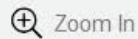
Settings

## Exhibit Display

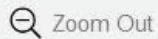
## Roux-en-Y gastric bypass



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Zoom In



Zoom Out



Reset



New



Existing



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Block Time Remaining: 00:15:55

TUTOR

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Feedback



Suspend



End Block



The normal small intestine is colonized with facultative anaerobes, lactobacilli, enterococci, and gram-positive aerobes. **Enteric bacteria** can **produce** vitamins (eg, **vitamin K, folate**), inhibit proliferation of surrounding pathogenic bacteria, and digest unabsorbed dietary sugars and convert them to fatty acids.

A Roux-en-Y gastric bypass surgery typically creates a small gastric pouch, which is removed from the remainder of the stomach and attached to the jejunum via a gastrojejunal anastomosis. The larger bypassed portion of the stomach and duodenum are reattached to the jejunum distally. This results in a closed-ended gastroduodenal limb, in which bacteria can proliferate and ferment any food that may be diverted into this segment. **Small intestinal bacterial overgrowth** (SIBO) is characterized by overproduction of vitamin K and folate, associated with nausea, bloating, abdominal discomfort, and malabsorption.

**(Choice A)** SIBO typically causes cobalamin (vitamin B<sub>12</sub>) deficiency due to decreased intestinal absorption of both free and intrinsic factor-bound vitamin B<sub>12</sub>. In addition, the bacteria can compete by utilizing the vitamin B<sub>12</sub>.

**(Choice C)** SIBO can cause iron deficiency due to decreased intestinal absorption, possibly through intestinal mucosal injury from bacterial toxins, unconjugated bile acids, or short-chain fatty acids.





absorption of both free and intrinsic factor-bound vitamin B<sub>12</sub>. In addition, the bacteria can compete by utilizing the vitamin B<sub>12</sub>.

**(Choice C)** SIBO can cause iron deficiency due to decreased intestinal absorption, possibly through intestinal mucosal injury from bacterial toxins, unconjugated bile acids, or short-chain fatty acids.

**(Choice D)** SIBO typically causes malabsorption of fat-soluble vitamins, including A, D, and E. However, vitamin K is usually normal or slightly increased due to increased bacterial synthesis.

**(Choice E)** In SIBO, zinc deficiency is typically due to small intestinal malabsorption. SIBO patients with diarrhea can also have increased zinc loss.

### Educational objective:

Gastric bypass surgery can cause small intestinal bacterial overgrowth (SIBO) due to excessive bacterial proliferation in the blind-ended gastroduodenal segment. SIBO results in deficiency of most vitamins (B<sub>12</sub>, A, D, and E) and iron, but increased production of folic acid and vitamin K.

### References

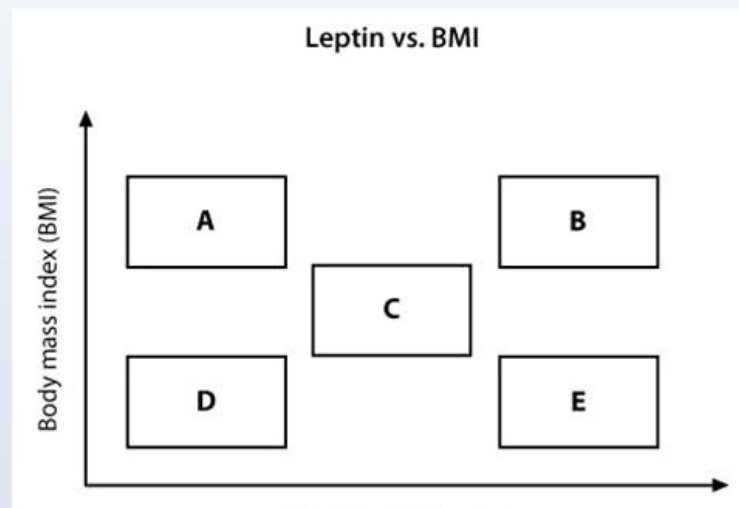
- Review article: small intestinal bacterial overgrowth--prevalence, clinical features, current and developing diagnostic tests, and treatment.

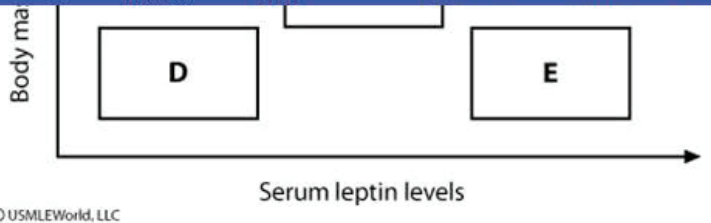






An investigator is studying weight regulation using experimental mouse models. Knockout mice are created with a homozygous mutation in the gene coding for the leptin receptor. This mutation prevents the receptor from binding leptin and initiating its normal signaling cascade. The knockout mice are allowed to feed at will, and their body mass index (BMI) and serum leptin levels are measured and compared with control mice. On the graph below, area C represents the normal relationship between BMI and leptin in a control mouse.



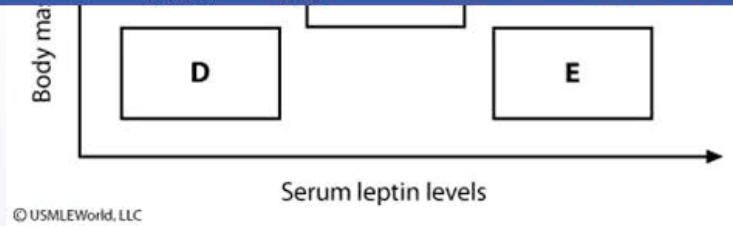


Which of the following areas represents the expected relationship between BMI and serum leptin levels in a leptin receptor mutant mouse?

- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit





Which of the following areas represents the expected relationship between BMI and serum leptin levels in a leptin receptor mutant mouse?

- ☐ A.A (15%)
- ☒ B.B (68%)
- ☐ C.C (1%)
- ☐ D.D (3%)
- ☐ E.E (10%)

Correct

68%



01 min, 10 secs



01/22/2021

Block Time Remaining: 00:17:05

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Feedback



Suspend



End Block





Leptin is a protein hormone that plays an important role in regulating appetite and metabolism. It is produced primarily in adipocytes, and large fat cells produce more leptin than small ones. Serum leptin concentrations are highly correlated with body fat content.

Leptin decreases food intake in the following important ways:

1. Leptin decreases the production of neuropeptide Y, a potent appetite stimulant, in the arcuate nucleus of the hypothalamus.
2. Leptin stimulates the production of proopiomelanocortin (POMC) in the arcuate nucleus. Alpha-melanocyte-stimulating hormone (alpha-MSH) is produced by cleavage of POMC and inhibits food intake.

The knockout mouse described is homozygous for a mutation in the gene encoding the leptin receptor (db/db), resulting in ineffective leptin signaling. As a result, these mice become hyperphagic and profoundly obese. As leptin production is normal in these mice, leptin levels are elevated due to the increased lipocyte mass. In contrast, mice that are homozygous for a mutation resulting in impaired leptin production (ob/ob) also become hyperphagic and profoundly obese, but their leptin levels are low (**Choice A**).

Human obesity resulting from mutations in the leptin receptor and the leptin gene has been described





production (ob/ob) also become hyperphagic and profoundly obese, but their leptin levels are low (**Choice A**).

Human obesity resulting from mutations in the leptin receptor and the leptin gene has been described. However, most obese individuals do not have either of these mutations. Instead, it is thought that the sustained elevation in leptin levels from the enlarged fat stores results in leptin desensitization. Thus, obese individuals become resistant to the effects of leptin in a manner similar to the development of insulin resistance in type 2 diabetes.

**(Choice D)** Low leptin and low BMI correlate with low adipocyte stores and may be seen after prolonged starvation.

**(Choice E)** With intact receptor signaling, elevated leptin levels (ie, from exogenous leptin administration) would result in weight loss.

### Educational objective:

Leptin is a protein hormone produced by adipocytes in proportion to the quantity of fat stored. Leptin acts on the arcuate nucleus of the hypothalamus to inhibit production of neuropeptide Y (decreasing appetite) and stimulate production of alpha-MSH (increasing satiety). Mutations in the leptin gene or receptor result in hyperphagia and profound obesity.





A 72-year-old woman comes to the office for follow-up of chronic abdominal pain. She has had several episodes of left lower quadrant pain requiring hospitalization. Despite treatment, her symptoms continue to recur. Elective surgery is performed and a segment of resected and opened sigmoid colon is shown below.





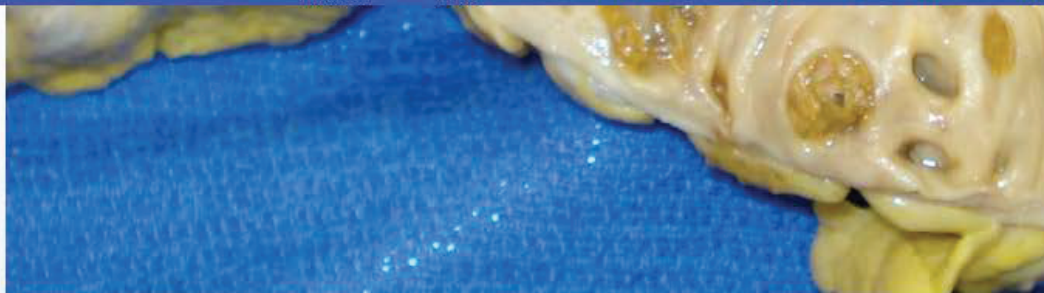


Which of the following most likely contributed to this patient's condition?

- ☐ A. Consumption of high-fiber foods
- ☐ B. Frequent consumption of seeds and nuts
- ☐ C. High dietary intake of fat and red meat
- ☐ D. Infection with *Helicobacter pylori*
- ☐ E. Prolonged and excessive alcohol intake

Submit





Which of the following most likely contributed to this patient's condition?

- ☐ A. Consumption of high-fiber foods (3%)
- ☐ B. Frequent consumption of seeds and nuts (13%)
- ☒ C. High dietary intake of fat and red meat (77%)
- ☐ D. Infection with *Helicobacter pylori* (1%)
- ☐ E. Prolonged and excessive alcohol intake (4%)

Correct

77%



40 secs



12/09/2020

Block Time Remaining: 00:17:45

TUTOR

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1



Feedback



Suspend



End Block

### Diverticular disease

<b>Etiology</b>	<ul style="list-style-type: none"><li>• Diverticulosis: ↑ intraluminal pressure causing herniation through points of weakness (vasa recta penetration)</li><li>• Diverticular bleeding: injury to exposed vasa recta</li><li>• Diverticulitis: trapped food particles &amp; ↑ intraluminal pressure causing microperforation</li></ul>
<b>Symptoms</b>	<ul style="list-style-type: none"><li>• Diverticulosis: none</li><li>• Diverticular bleeding: painless hematochezia</li><li>• Diverticulitis: left lower quadrant pain, nausea, vomiting, fever</li></ul>
<b>Risk factors</b>	<ul style="list-style-type: none"><li>• Diet high in red meat &amp; fat &amp; low in fiber</li><li>• Obesity, physical inactivity, smoking</li></ul>

This patient's gross pathology demonstrates multiple **sac-like outpouchings** from the sigmoid colon, which is consistent with diverticulosis. **Diverticulosis** occurs due to excessive colonic contractions that cause increased intraluminal pressure; this forces the mucosa and submucosa to herniate through the muscularis at naturally weak areas where the vasa recta penetrate. It is an exceedingly common disorder, particularly





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



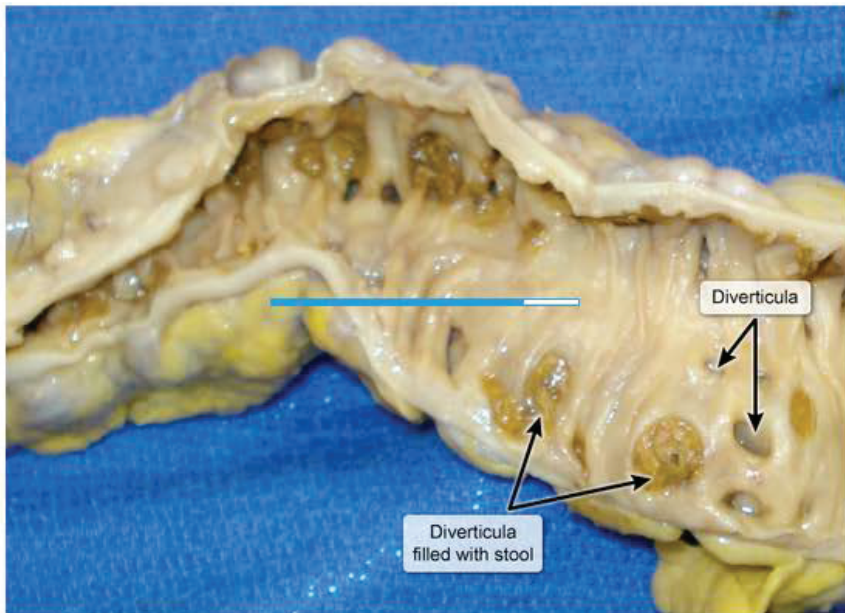
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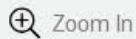
Settings

### Exhibit Display

#### Colonic diverticulosis



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Zoom In



Zoom Out



Reset



New



Existing



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Block Time Remaining: 00:17:45

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1



Feedback



Suspend



End Block



Factors • Obesity, physical inactivity, smoking

This patient's gross pathology demonstrates multiple **sac-like outpouchings** from the sigmoid colon, which is consistent with diverticulosis. **Diverticulosis** occurs due to excessive colonic contractions that cause increased intraluminal pressure; this forces the mucosa and submucosa to herniate through the muscularis at naturally weak areas where the vasa recta penetrate. It is an exceedingly common disorder, particularly in Western nations, and its incidence increases with age.

Diverticulosis may be clinically silent, but up to 30% of patients develop complications, including diverticular bleeding and diverticulitis. **Diverticular bleeding** occurs with injury to the exposed vasa recta within the colonic lumen and typically presents with **painless** hematochezia. **Diverticulitis** is caused by trapped food particles or excessive intraluminal pressure within the diverticula, leading to focal necrosis and microperforation. Patients develop **abdominal pain** (usually in the **left lower quadrant**), fever, nausea and vomiting, and alterations in bowel habits (eg, diarrhea, constipation). Diverticulitis is typically managed with antibiotics and bowel rest; however, surgery may be required for recurrent disease.

The risk for diverticular disease is increased by dietary factors, including **diets high in red meat**, high in **fat**, and low in fiber (**Choice A**). Other risk factors include obesity, physical inactivity, and smoking.

(**Choice B**) Although previously thought to be associated with diverticular diseases, the ingestion of nuts,





fat, and low in fiber (**Choice A**). Other risk factors include obesity, physical inactivity, and smoking.

(**Choice B**) Although previously thought to be associated with diverticular diseases, the ingestion of nuts, seeds, and popcorn is not correlated with increased risk of diverticulosis, diverticular bleeding, or diverticulitis.

(**Choice D**) *Helicobacter pylori* infection is associated with peptic ulcer and gastric cancer but does not increase the risk of diverticular disease.

(**Choice E**) Excessive alcohol intake is associated with liver cirrhosis and squamous cell carcinoma of the esophagus; it is not associated with diverticular disease.

### Educational objective:

Colonic diverticulosis refers to multiple sac-like outpouchings within the sigmoid colon. Complications include diverticular bleeding and diverticulitis. Risk factors for diverticulosis include a diet high in red meat and fat and low in fiber, as well as obesity and physical inactivity.

### References

- [Diagnosis and management of acute diverticulitis.](#)







A 54-year-old man with a history of hepatitis C infection is brought to the emergency department by his wife after several episodes of vomiting bright red blood. He is admitted to the hospital and the appropriate treatment is initiated. During morning rounds the next day, the patient is disoriented and cannot identify the month or his current location. Physical examination shows significant abdominal distention and gynecomastia. Repetitive flicking motions of the hands are seen when the patient is asked to outstretch his arms and dorsiflex his wrists. Which of the following is most likely contributing to this patient's altered mental status?

- ☐ A. Accumulation of blood urea nitrogen
- ☐ B. Bacterial infection of the meninges
- ☐ C. Decreased gamma-aminobutyric acid receptor stimulation
- ☐ D. Increased absorption of nitrogenous substances by the gut
- ☐ E. Occlusion of the middle cerebral artery

**Submit**

Block Time Remaining: 00:17:46

TUTOR

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1



Feedback



Suspend



End Block



A 54-year-old man with a history of hepatitis C infection is brought to the emergency department by his wife after several episodes of vomiting bright red blood. He is admitted to the hospital and the appropriate treatment is initiated. During morning rounds the next day, the patient is disoriented and cannot identify the month or his current location. Physical examination shows significant abdominal distention and gynecomastia. Repetitive flicking motions of the hands are seen when the patient is asked to outstretch his arms and dorsiflex his wrists. Which of the following is most likely contributing to this patient's altered mental status?

- ☐ A. Accumulation of blood urea nitrogen (46%)
- ☐ B. Bacterial infection of the meninges (0%)
- ☐ C. Decreased gamma-aminobutyric acid receptor stimulation (8%)
- ☒ D. Increased absorption of nitrogenous substances by the gut (43%)
- ☐ E. Occlusion of the middle cerebral artery (0%)





## Hepatic encephalopathy

### Precipitating factors

- Drugs (eg, sedatives, narcotics)
- Hypovolemia (eg, diarrhea)
- Electrolyte changes (eg, hypokalemia)
- ↑ Nitrogen load (eg, GI bleeding)
- Infection (eg, pneumonia, UTI, SBP)
- Portosystemic shunting (eg, TIPS)

### Clinical presentation

- Sleep pattern changes
- Altered mental status
- Ataxia
- Asterixis

### Treatment

- Correct precipitating causes (eg, fluids, antibiotics)
- ↓ Blood ammonia concentration (eg, lactulose, rifaximin)

**GI** = gastrointestinal; **SBP** = spontaneous bacterial peritonitis; **TIPS** = transjugular intrahepatic portosystemic







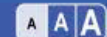
shunt; **UTI** = urinary tract infection.

This patient with cirrhosis (hepatitis C infection, abdominal distention, gynecomastia) most likely developed **hepatic encephalopathy** due to his recent **gastrointestinal (GI) bleed**. Hepatic encephalopathy refers to a reversible decline in neurologic function that occurs due to failure of the liver to metabolize waste products such as ammonia. Ammonia is normally produced by the GI tract as a result of enterocytic catabolism of glutamine and colonic bacterial catabolism of dietary protein. GI bleeding causes **increased nitrogen delivery** to the gut in the form of hemoglobin, which is then converted into ammonia and absorbed into the bloodstream. The ammonia then enters the liver through the portal vein and is detoxified to urea.

In chronic liver failure, hepatocyte dysfunction and the shunting of blood through portosystemic collaterals impair the liver's detoxification ability. This leads to **accumulation of ammonia** and other neurotoxins in the circulation, causing altered amino acid transport across the blood-brain barrier, impaired neurotransmitter metabolism, and depressed cerebral glucose metabolism. These and other factors result in **increased inhibitory neurotransmission** (eg,  $\gamma$ -aminobutyric acid [GABA]) and **impaired excitatory neurotransmitter release** (eg, glutamate, catecholamines).

In patients with hepatic encephalopathy, lowering of blood ammonia levels is typically accomplished with





In patients with hepatic encephalopathy, lowering of blood ammonia levels is typically accomplished with oral administration of a disaccharide (eg, **lactulose**). Bacterial action on lactulose results in acidification of colonic contents, which then converts absorbable ammonia into nonabsorbable ammonium ions, trapping it in the stool and thereby increasing fecal nitrogen excretion.

**(Choice A)** Accumulation of blood urea nitrogen (BUN) is suggestive of renal failure, heart failure, or dehydration. In healthy patients, GI bleeding can also cause a rapid increase in BUN. However, this patient has cirrhosis, which is associated with decreased BUN because ammonia cannot be efficiently converted to urea by the failing liver.

**(Choice B)** Bacterial meningitis presents with altered mental status, fever, nuchal rigidity, headache, and photophobia. In addition, asterixis (flapping tremor) is specific for metabolic encephalopathies.

**(Choice C)** The altered mental status seen in hepatic encephalopathy is due to increased (not decreased) activity of the GABA neurotransmitter system. This enhanced activity is caused by increased GABA receptor affinity and alterations in neurosteroid synthesis rather than increased GABA production.

**(Choice E)** The middle cerebral artery is the largest cerebral artery and the one most commonly involved in cerebrovascular accidents. This patient's presentation is suggestive of hepatic encephalopathy rather than stroke.







patient has cirrhosis, which is associated with decreased BUN because ammonia cannot be efficiently converted to urea by the failing liver.

**(Choice B)** Bacterial meningitis presents with altered mental status, fever, nuchal rigidity, headache, and photophobia. In addition, asterix (flapping tremor) is specific for metabolic encephalopathies.

**(Choice C)** The altered mental status seen in hepatic encephalopathy is due to increased (not decreased) activity of the GABA neurotransmitter system. This enhanced activity is caused by increased GABA receptor affinity and alterations in neurosteroid synthesis rather than increased GABA production.

**(Choice E)** The middle cerebral artery is the largest cerebral artery and the one most commonly involved in cerebrovascular accidents. This patient's presentation is suggestive of hepatic encephalopathy rather than stroke.

### Educational objective:

Hepatic encephalopathy is caused by increased levels of ammonia and other neurotoxins in the circulation that lead to increased inhibitory neurotransmission and impaired excitatory neurotransmitter release.

Hepatic encephalopathy is frequently precipitated by a stressor (eg, gastrointestinal bleeding, infection) that increases blood ammonia levels.

### References







order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 54-year-old man comes to the emergency department after an episode of bloody vomiting. He has had no fever, chills, abdominal pain, diarrhea, or constipation. The patient has a history of alcohol abuse with multiple previous hospital admissions due to alcohol withdrawal and generalized tonic-clonic seizures. He also has a history of intravenous drug abuse and is currently enrolled in a methadone maintenance program. Blood pressure is 96/62 mm Hg and pulse is 102/min. On examination, the patient appears comfortable but develops dizziness when asked to sit up. There is no jugular venous distension. The abdomen is distended with dullness to percussion at both flanks. The liver is enlarged on palpation, and the tip of the spleen is also palpable. There is trace pedal edema. Laboratory studies show:

Hemoglobin	9.7 g/dL
Mean corpuscular volume	98 fL
Leukocytes	5,000/mm <sup>3</sup>
Platelets	78,000/mm <sup>3</sup>

Item 1 of 2





Hemoglobin 9.7 g/dL

Mean corpuscular volume 98 fL

Leukocytes 5,000/mm<sup>3</sup>

Platelets 78,000/mm<sup>3</sup>

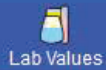
### Item 1 of 2

Histopathologic examination of this patient's spleen is most likely to show which of the following?

- ☐ A. Extramedullary hematopoiesis
- ☐ B. Histiocytic proliferation
- ☐ C. Lymphoid follicle expansion
- ☐ D. Metastatic deposits
- ☐ E. Red pulp expansion

Submit





Mean corpuscular volume 98 fL

Leukocytes 5,000/mm<sup>3</sup>

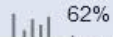
Platelets 78,000/mm<sup>3</sup>

### Item 1 of 2

Histopathologic examination of this patient's spleen is most likely to show which of the following?

- ☐ A. Extramedullary hematopoiesis (25%)
- ☐ B. Histiocytic proliferation (5%)
- ☐ C. Lymphoid follicle expansion (4%)
- ☐ D. Metastatic deposits (1%)
- ☒ E. Red pulp expansion (62%)

Correct



62%



01 min, 08 secs

Time Spent



01/23/2021

Last Updated

Block Time Remaining: 00:19:44

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Feedback

Suspend

End Block





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient with a history of significant alcohol and intravenous drug abuse has evidence of **alcoholic liver disease** (ALD). His hematemesis, orthostatic symptoms, and normocytic anemia are likely due to acute bleeding from esophageal varices. Although chronic gastrointestinal blood loss can cause microcytic anemia due to depletion of iron stores and reduced hemoglobin synthesis, acute hemorrhage (as in this patient) is usually associated with normal mean corpuscular volume. ALD also causes thrombocytopenia due to decreased platelet production, increased destruction, and splenic sequestration.

Fibrosis and distortion of intrahepatic vasculature in ALD obstructs blood flow through the liver, leading to **portal hypertension**. Because the splenic vein is part of the portal circulation, any condition that causes portal hypertension can lead to **splenomegaly** with congestive hypersplenism. Venous congestion causes apparent **expansion of the red pulp** of the spleen, which is composed of blood-filled sinuses and cords lined by reticuloendothelial-type cells.

**(Choice A)** Extramedullary hematopoiesis results when hematopoietic precursor cells are displaced from the bone marrow and infiltrate the liver and spleen preferentially, resulting in splenomegaly. A common condition in which this occurs is myelofibrosis.

**(Choices B and D)** Histiocytic proliferation can cause splenomegaly in the setting of Langerhans cell histiocytosis (formerly known as histiocytosis X), but this is a rare disease with highest incidence in



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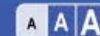
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End Block



condition in which this occurs is myelofibrosis.

**(Choices B and D)** Histiocytic proliferation can cause splenomegaly in the setting of Langerhans cell histiocytosis (formerly known as histiocytosis X), but this is a rare disease with highest incidence in childhood. Metastatic tumors (eg, lung, breast, colorectal cancer) can infiltrate the spleen and lead to hypersplenism, but this patient has no history of malignancy. Given this patient's substance abuse history, ALD is much more likely.

**(Choice C)** Lymphoid follicle expansion can cause hypersplenism in the setting of systemic infections (eg, infectious mononucleosis) or as a result of immunologic diseases (eg, systemic lupus erythematosus, rheumatoid arthritis [Felty syndrome]).

### Educational objective:

Portal hypertension, as seen in alcoholic liver disease, produces splenomegaly by causing congestion of blood within the spleen, which produces expansion of the red pulp.

Pathology

Gastrointestinal & Nutrition

Cirrhosis

Subject

System

Topic

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**Item 2 of 2**

After initial stabilization with intravenous fluids and blood products, the patient develops another bout of bloody emesis. Urgent upper gastrointestinal endoscopy confirms esophageal varices. Which of the following peptides is most likely to immediately decrease the portal venous pressure in this patient?

- ☐ A. Cholecystokinin
- ☐ B. Glucagon
- ☐ C. Pentagastrin
- ☐ D. Secretin
- ☐ E. Somatostatin

**Submit**





## Item 2 of 2

After initial stabilization with intravenous fluids and blood products, the patient develops another bout of bloody emesis. Urgent upper gastrointestinal endoscopy confirms esophageal varices. Which of the following peptides is most likely to immediately decrease the portal venous pressure in this patient?

- ☐ A. Cholecystokinin (3%)
- ☐ B. Glucagon (4%)
- ☐ C. Pentagastrin (3%)
- ☐ D. Secretin (1%)
- ☒ E. Somatostatin (87%)

Correct

 87%  
Answered correctly

 22 secs  
Time Spent

 01/23/2021  
Last Updated





Prolonged **portal hypertension** in alcoholic liver disease can cause venous engorgement and dilation (ie, **varices**) at sites of portocaval anastomosis in the esophagus, rectum, umbilicus, and retroperitoneum. Subsequent rupture of esophageal varices can cause rapid blood loss and carries high mortality.

Acute management of variceal hemorrhage requires rapid lowering of portal pressure. **Somatostatin** and **octreotide** (a long-acting somatostatin analog) inhibit the release of endogenous hormones (eg, glucagon, vasoactive intestinal peptide) that induce splanchnic vasodilation, thereby indirectly **reducing portal blood flow**. Vasopressin directly causes splanchnic vasoconstriction and also can lower portal flow in acute variceal hemorrhage, but its use is limited by systemic vasoconstriction.

**(Choices A, B, and D)** Glucagon causes splanchnic vasodilation, raising portal pressure and worsening variceal bleeding. Cholecystokinin induces contraction of the gallbladder and expulsion of pancreatic exocrine secretions into the duodenum, whereas the primary function of secretin is to alkalinize the duodenal contents; both of these hormones increase glucagon secretion and would therefore be counterproductive in this setting.

**(Choice C)** Pentagastrin is a synthetic gastrin analog that stimulates secretion of gastric acid. Its primary clinical use is as a diagnostic agent; pentagastrin induces a significant rise in calcitonin secretion in patients with medullary carcinoma of the thyroid and serotonin secretion in patients with carcinoid tumors.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choices A, B, and D)** Glucagon causes splanchnic vasodilation, raising portal pressure and worsening variceal bleeding. Cholecystokinin induces contraction of the gallbladder and expulsion of pancreatic exocrine secretions into the duodenum, whereas the primary function of secretin is to alkalinize the duodenal contents; both of these hormones increase glucagon secretion and would therefore be counterproductive in this setting.

**(Choice C)** Pentagastrin is a synthetic gastrin analog that stimulates secretion of gastric acid. Its primary clinical use is as a diagnostic agent; pentagastrin induces a significant rise in calcitonin secretion in patients with medullary carcinoma of the thyroid and serotonin secretion in patients with carcinoid tumors.

### Educational objective:

Acute management of variceal hemorrhage requires rapid lowering of portal pressure. Somatostatin and octreotide (a long-acting somatostatin analog) inhibit the release of hormones that induce splanchnic vasodilation, indirectly causing splanchnic vasoconstriction and reduced portal blood flow.

### References

- Portal hypertension and variceal hemorrhage.
- Acute variceal bleeding.



0



Feedback



Suspend



End Block





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 65-year-old man comes to the office with dysphagia. For the last 3 months, he has relied on protein shakes and juices for nourishment as he has had difficulty swallowing solid foods. He has also had a diminished appetite and an estimated weight loss of 9.1 kg (20 lb). Medical history includes hyperlipidemia, emphysema, and previous episodes of pancreatitis. Family history includes lung cancer in his mother. The patient smoked a pack of cigarettes daily for 50 years but quit 2 years ago. He has been drinking a fifth (750 mL) of vodka weekly for the last decade. Vital signs are normal. BMI is 19.2 kg/m<sup>2</sup>. Temporal wasting is present but physical examination is otherwise unremarkable. Upper endoscopy reveals a 4-cm mass in the middle third of the esophagus, and several biopsies are taken. Thoracic imaging reveals mediastinal lymphadenopathy. Histologic evaluation of the biopsy specimens will most likely show which of the following in this patient?

- ☐ A. Intestinal cells without dysplasia
- ☐ B. Irregular glandular cells with tissue invasion
- ☐ C. Keratin pearls and intercellular bridges
- ☐ D. Myocytes with prominent atypia
- ☐ E. Spindle cells expressing CD117



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shakes and juices for nourishment as he has had difficulty swallowing solid foods. He has also had a diminished appetite and an estimated weight loss of 9.1 kg (20 lb). Medical history includes hyperlipidemia, emphysema, and previous episodes of pancreatitis. Family history includes lung cancer in his mother. The patient smoked a pack of cigarettes daily for 50 years but quit 2 years ago. He has been drinking a fifth (750 mL) of vodka weekly for the last decade. Vital signs are normal. BMI is 19.2 kg/m<sup>2</sup>. Temporal wasting is present but physical examination is otherwise unremarkable. Upper endoscopy reveals a 4-cm mass in the middle third of the esophagus, and several biopsies are taken. Thoracic imaging reveals mediastinal lymphadenopathy. Histologic evaluation of the biopsy specimens will most likely show which of the following in this patient?

- ☐ A. Intestinal cells without dysplasia
- ☐ B. Irregular glandular cells with tissue invasion
- ☐ C. Keratin pearls and intercellular bridges
- ☐ D. Myocytes with prominent atypia
- ☐ E. Spindle cells expressing CD117





emphysema, and previous episodes of pancreatitis. Family history includes lung cancer in his mother. The patient smoked a pack of cigarettes daily for 50 years but quit 2 years ago. He has been drinking a fifth (750 mL) of vodka weekly for the last decade. Vital signs are normal. BMI is 19.2 kg/m<sup>2</sup>. Temporal wasting is present but physical examination is otherwise unremarkable. Upper endoscopy reveals a 4-cm mass in the middle third of the esophagus, and several biopsies are taken. Thoracic imaging reveals mediastinal lymphadenopathy. Histologic evaluation of the biopsy specimens will most likely show which of the following in this patient?

- ☐ A. Intestinal cells without dysplasia (0%)
- ☐ B. Irregular glandular cells with tissue invasion (13%)
- ☒ C. Keratin pearls and intercellular bridges (83%)
- ☐ D. Myocytes with prominent atypia (1%)
- ☐ E. Spindle cells expressing CD117 (1%)

Correct

83%



49 secs



01/07/2021

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### Squamous cell carcinoma of the esophagus

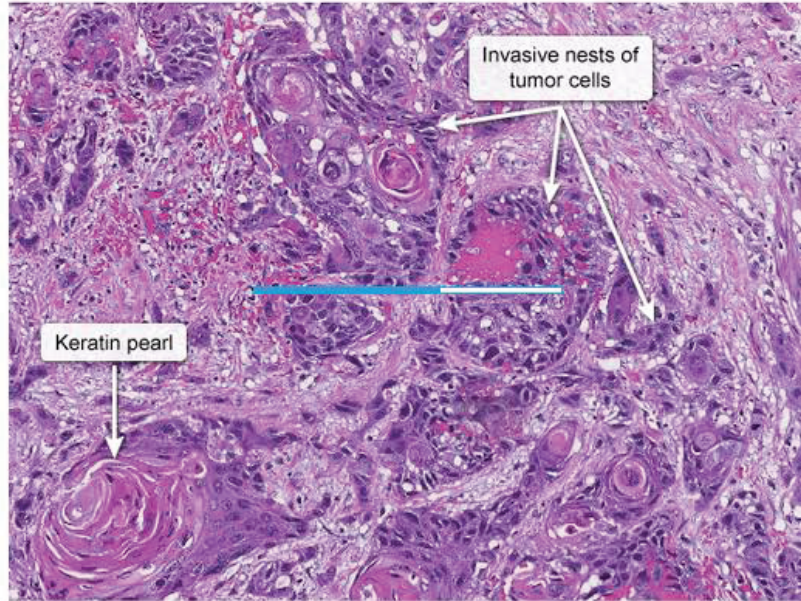
<b>Risk factors</b>	<ul style="list-style-type: none"><li>• Alcohol, smoking, foods containing N-nitroso</li><li>• Age &gt;50</li></ul>
<b>Location</b>	<ul style="list-style-type: none"><li>• Proximal two-thirds of esophagus (most common in the middle third)</li><li>• Associated mediastinal lymphadenopathy</li></ul>
<b>Histopathology</b>	<ul style="list-style-type: none"><li>• Sheets of eosinophilic squamous cells</li><li>• Keratin pearls, intercellular bridges</li></ul>

This patient with a mid-esophageal mass and mediastinal lymphadenopathy likely has **squamous cell carcinoma** (SCC) of the esophagus. SCC is characterized by sheets or nests of atypical squamous cells with abundant eosinophilic cytoplasm and may show large, bizarre nuclei with atypical mitoses; **keratin formation** (**keratin pearls**) and **intercellular bridges** are common. Malignant cells are often seen invading the submucosa and surrounding structures.

The esophagus can be subdivided (based on anatomy and embryonic formation) into thirds; malignancies occur at different frequencies within each segment.

Exhibit Display

Squamous cell carcinoma



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Previous



Next



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Notes



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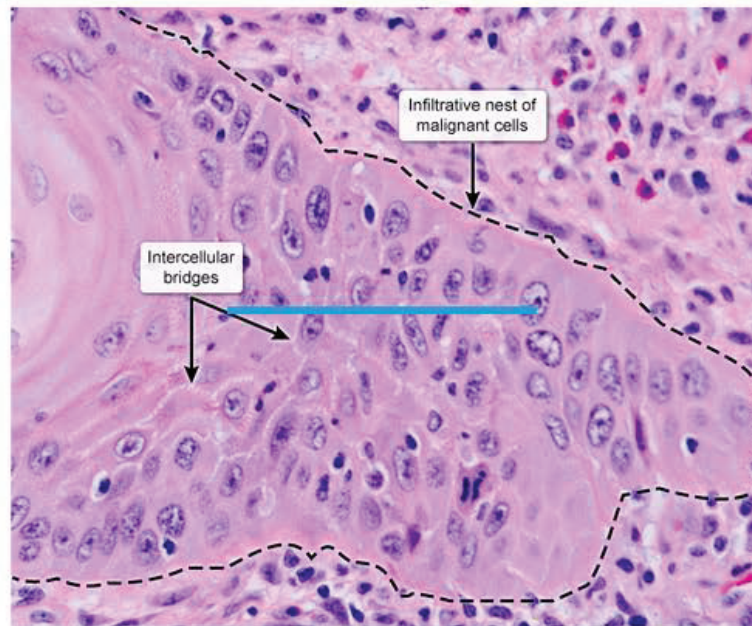
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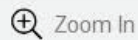
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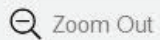
## Squamous cell carcinoma



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The esophagus can be subdivided (based on anatomy and embryonic formation) into thirds; malignancies occur at different frequencies within each segment.

- Proximal and middle third: SCC is more common, and occurs at the highest frequency in the **middle third**. Lymphatics drain to mediastinal nodes; metastatic disease may present with **mediastinal lymphadenopathy**.
- Distal third: Adenocarcinoma is more common. Lymphatics drain caudally to the gastric and celiac nodes; metastatic disease may present with abdominal lymphadenopathy.

**Adenocarcinoma** is characterized by invasive patches of dysplastic, mucin-producing cells that form glands. It typically occurs as a consequence of chronic gastroesophageal reflux disease and is preceded by **Barrett esophagus** (replacement of the normal esophagus with nondysplastic columnar intestinal cells) **(Choices A and B)**.

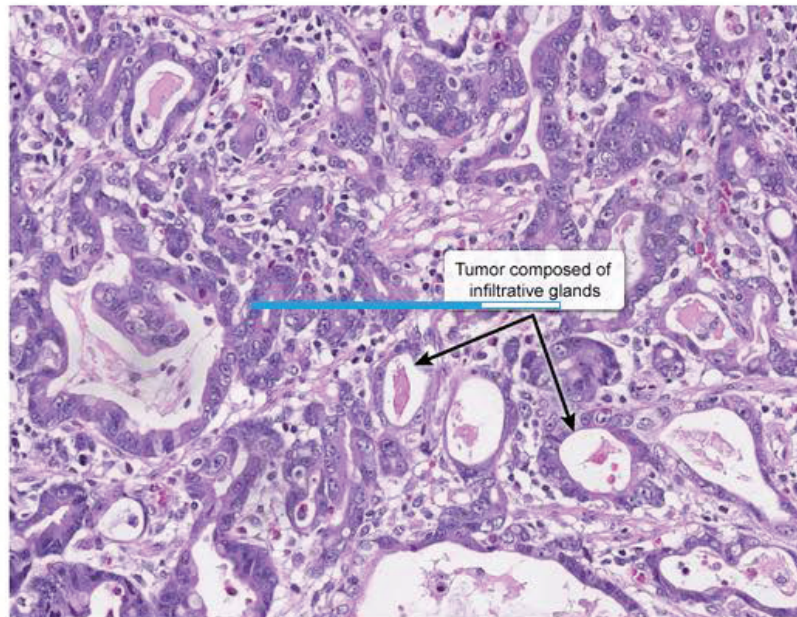
**(Choices D and E)** **Leiomyosarcoma** demonstrates myocyte atypia on histology. **Gastrointestinal stromal tumors** are often composed of uniform spindle cells that overexpress CD117. These malignancies occur more commonly in the stomach and small intestine and are rare in the esophagus.

**Educational objective:**



### Exhibit Display

#### Esophageal adenocarcinoma



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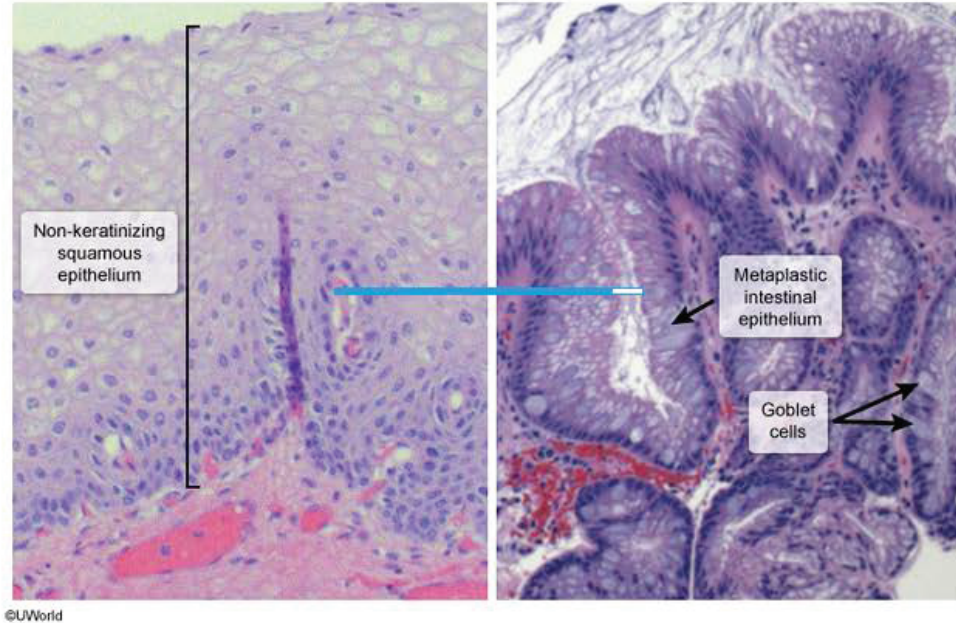
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Exhibit Display

Normal esophagus

Barrett esophagus



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



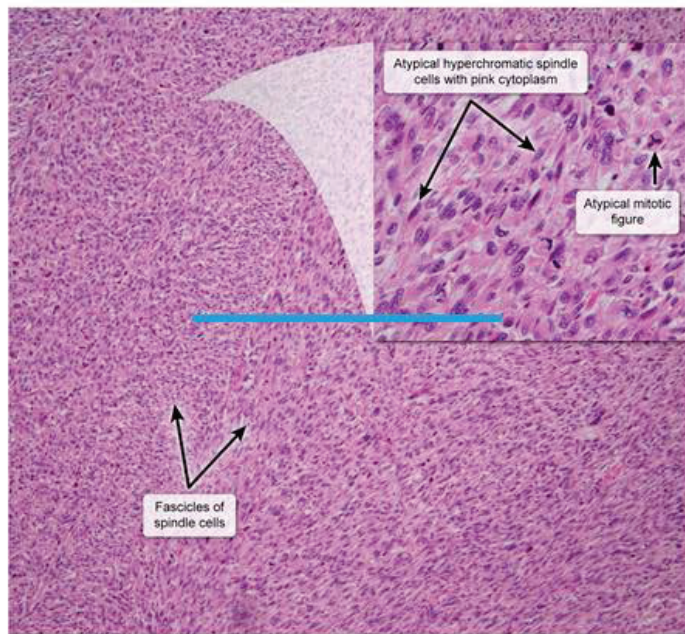
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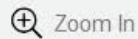
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## Exhibit Display

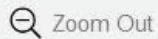
## Leiomyosarcoma



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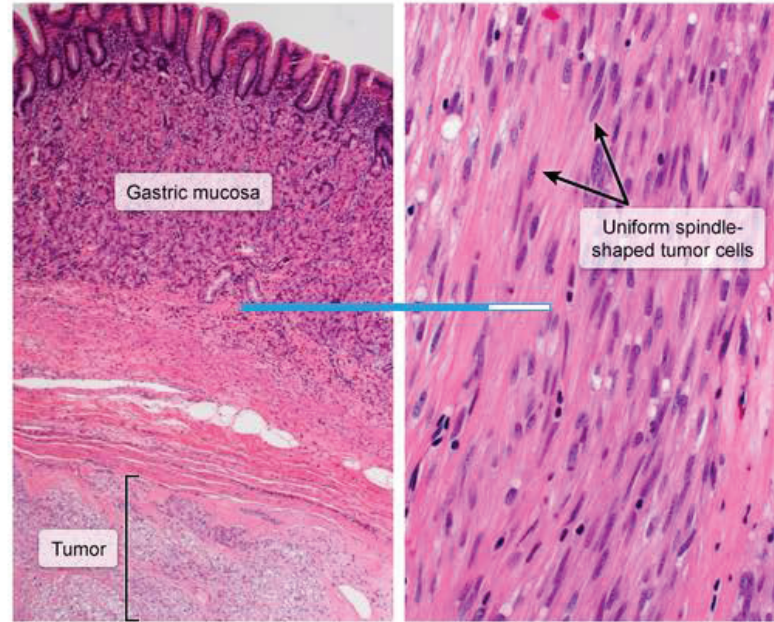
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### Exhibit Display

#### Gastrointestinal stromal tumor



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### lymphadenopathy.

- Distal third: Adenocarcinoma is more common. Lymphatics drain caudally to the gastric and celiac nodes; metastatic disease may present with abdominal lymphadenopathy.

**Adenocarcinoma** is characterized by invasive patches of dysplastic, mucin-producing cells that form glands. It typically occurs as a consequence of chronic gastroesophageal reflux disease and is preceded by **Barrett esophagus** (replacement of the normal esophagus with nondysplastic columnar intestinal cells) **(Choices A and B).**

**(Choices D and E)** **Leiomyosarcoma** demonstrates myocyte atypia on histology. **Gastrointestinal stromal tumors** are often composed of uniform spindle cells that overexpress CD117. These malignancies occur more commonly in the stomach and small intestine and are rare in the esophagus.

### Educational objective:

Esophageal squamous cell carcinoma presents mostly in the proximal two-thirds of the esophagus and frequently metastasizes to the mediastinal lymph nodes. Histology characteristically shows sheets of atypical squamous cells with keratin pearls and intercellular bridges.







A 45-year-old man comes to the emergency department due to sudden-onset vomiting and severe upper abdominal pain that radiates to his back. The patient's total bilirubin is 0.9 mg/dL, aspartate aminotransferase (AST) is 98 U/L, alanine aminotransferase (ALT) is 32 U/L, and alkaline phosphatase is 98 U/L. Serum lipase is markedly increased. Abdominal ultrasound reveals a normal gallbladder and common bile duct. The diagnosis of acute pancreatitis is made, and a specific etiology is established. Which of the following additional laboratory findings is most specific for the underlying cause of this patient's pancreatitis?

- ☐ A. Mean corpuscular volume of 108 fL
- ☐ B. Serum calcium level of 8 mg/dL
- ☐ C. Serum glucose level of 180 mg/dL
- ☐ D. Serum sodium level of 150 mEq/L
- ☐ E. White blood cell count of 22,000/mm<sup>3</sup>

**Submit**



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 45-year-old man comes to the emergency department due to sudden-onset vomiting and severe upper abdominal pain that radiates to his back. The patient's total bilirubin is 0.9 mg/dL, aspartate aminotransferase (AST) is 98 U/L, alanine aminotransferase (ALT) is 32 U/L, and alkaline phosphatase is 98 U/L. Serum lipase is markedly **increased**. Abdominal ultrasound reveals a normal gallbladder and common bile duct. The diagnosis of acute pancreatitis is made, and a specific etiology is established. Which of the following additional laboratory findings is most specific for the underlying cause of this patient's pancreatitis?

- ☒ A. Mean corpuscular volume of 108 fL (34%)
- ☐ B. Serum calcium level of 8 mg/dL (24%)
- ☐ C. Serum glucose level of 180 mg/dL (16%)
- ☐ D. Serum sodium level of 150 mEq/L (3%)
- ☐ E. White blood cell count of 22,000/mm<sup>3</sup> (20%)



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



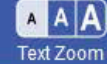
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Text Zoom



Settings

This patient's **acute pancreatitis** is likely related to **alcohol abuse** given his **>2 AST:ALT ratio** and **absence of gallstones** on abdominal ultrasound. After gallstones, alcohol abuse is the second most common cause of acute pancreatitis. Ethanol induces pancreatic secretions with a high protein concentration and low fluid content. These viscous secretions are prone to precipitate and form plugs that can obstruct the lumina of the pancreatic ductules. Alcohol also causes spasms of the sphincter of Oddi and has a direct toxic effect on the acinar cells.

Alcohol-related acute pancreatitis is clinically **indistinguishable** from pancreatitis due to other causes. However, chronic alcohol use causes a number of systemic effects due to both the direct toxic actions of ethanol and alcoholism-associated vitamin deficiencies. Even in the absence of anemia, **macrocytosis** (mean corpuscular volume >100 fL) is often seen and is likely related to poor nutrition (eg, folate deficiency), liver disease, and/or direct toxicity of alcohol on the marrow.

**(Choice B)** In severe acute pancreatitis, necrosis can spread into the retroperitoneal fat, omentum, mesentery, and even beyond the abdominal cavity. Large amounts of calcium bind to the released free fatty acids, forming soaps that are deposited in the areas of necrosis, which may result in hypocalcemia. However, this is a nonspecific finding that can occur with pancreatitis of any etiology, not just alcoholic pancreatitis.



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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

pancreatitis.

**(Choice C)** Inflammation in acute pancreatitis may lead to dysfunction of the pancreatic islets with decreased secretion of insulin, resulting in hyperglycemia. This is a nonspecific finding that can occur with pancreatitis of any etiology, not just alcoholic pancreatitis.

**(Choice D)** Hyponatremia may occur in the setting of severe acute pancreatitis due to large third-space fluid loss (ie, interstitial fluid accumulation) and decreased water intake, causing subsequent hypovolemia and renal sodium retention. This finding is also not specific for alcoholic pancreatitis.

**(Choice E)** An increased white blood cell count is a nonspecific marker of inflammation and may occur with pancreatitis of any etiology.

### Educational objective:

After gallstones, alcohol abuse is the second most common cause of acute pancreatitis. Macrocytosis and an AST:ALT ratio  $>2$  are indirect indicators of chronic alcohol consumption. Alcohol-related macrocytosis can occur independently of folate deficiency.

### References

- [Pathophysiology of alcoholic pancreatitis: an overview.](#)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 72-year-old man develops mild abdominal pain and bloody diarrhea after undergoing urgent cholecystectomy. The surgery was complicated by an episode of hypotension that was treated with bolus intravenous crystalloid fluids. The patient had no previous gastrointestinal bleeding. His last colonoscopy 10 years ago was normal. Past medical history is notable for hypertension, hyperlipidemia, type 2 diabetes mellitus, and a myocardial infarction 7 years ago. The patient smoked for 40 years and quit after the myocardial infarction. Colonoscopy would most likely show pathology in which of the following portions of the large bowel?

- ☐ A. Ascending colon
- ☐ B. Cecum
- ☐ C. Hepatic flexure
- ☐ D. Rectosigmoid junction
- ☐ E. Mid-transverse colon

**Submit**

Block Time Remaining: 00:21:37

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Settings

A 72-year-old man develops mild abdominal pain and bloody diarrhea after undergoing urgent cholecystectomy. The surgery was complicated by an episode of hypotension that was treated with bolus intravenous crystalloid fluids. The patient had no previous gastrointestinal bleeding. His last colonoscopy 10 years ago was normal. Past medical history is notable for hypertension, hyperlipidemia, type 2 diabetes mellitus, and a myocardial infarction 7 years ago. The patient smoked for 40 years and quit after the myocardial infarction. Colonoscopy would most likely show pathology in which of the following portions of the large bowel?

- ☐ A. Ascending colon (10%)
- ☐ B. Cecum (4%)
- ☐ C. Hepatic flexure (22%)
- ☒ D. Rectosigmoid junction (43%)
- ☐ E. Mid-transverse colon (18%)







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

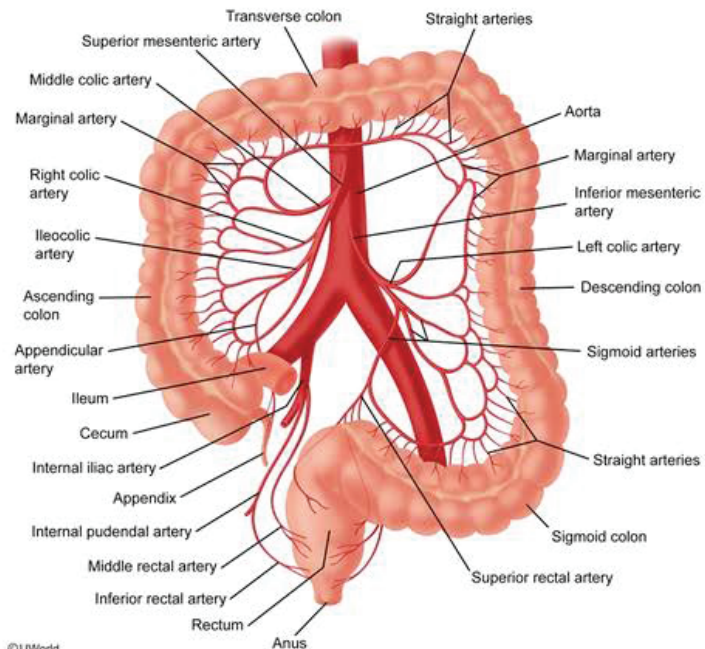
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## Exhibit Display

## Arteries of the large intestine



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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient with abdominal pain and bloody diarrhea following a complicated surgical procedure likely has acute nonocclusive **ischemic colitis**. The colon receives blood from the marginal artery of the colon (artery of Drummond), an anastomotic system of arteries that is in turn supplied by the superior (SMA) and inferior (IMA) mesenteric artery systems. The distal colon receives blood also from the internal iliac artery.

In low-flow states, as may be seen in severe hypotension in patients with underlying arterial insufficiency (eg, diabetes, atherosclerotic arterial disease), **nonocclusive ischemia** may occur at the margins of the anastomotic distributions. These "**watershed**" areas are primarily in the left colon at the **splenic flexure** (border between SMA and IMA supply) and **rectosigmoid junction** (border between sigmoid artery and superior rectal artery). Less commonly, **occlusive ischemia** can also be caused by thromboembolic (eg, hypercoagulable states, atrial fibrillation) or atheroembolic (eg, aortic instrumentation) events.

Impaired perfusion to the bowel leads to ischemia and necrosis of the intestinal wall. Complications can include acidosis, sepsis, gangrene, and perforation. Colonoscopy will reveal pale mucosa and petechial hemorrhages.

**(Choices A, B, C, and E)** The ascending colon, cecum, hepatic flexure, and most of the transverse colon are supplied by branches of the SMA. Mesenteric ischemia in these areas is significantly less common than in the watershed areas of the left colon. Ischemia is also uncommon in the rectum, which receives



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

hypotensive states, arterial hypotension, or other conditions (eg, acute instrumentation) events.

Impaired perfusion to the bowel leads to ischemia and necrosis of the intestinal wall. Complications can include acidosis, sepsis, gangrene, and perforation. Colonoscopy will reveal pale mucosa and petechial hemorrhages.

**(Choices A, B, C, and E)** The ascending colon, cecum, hepatic flexure, and most of the transverse colon are supplied by branches of the SMA. Mesenteric ischemia in these areas is significantly less common than in the watershed areas of the left colon. Ischemia is also uncommon in the rectum, which receives collateral blood supply via the rectal arteries.

### Educational objective:

The splenic flexure and rectosigmoid junction lie between regions of perfusion of major arteries. These "watershed" areas are susceptible to ischemic damage during hypotensive states, especially in patients with underlying arterial insufficiency.

### References

- [Clinical approach to colonic ischemia.](#)

Pathology

Gastrointestinal &amp; Nutrition

Colonic ischemia

Subject

System

Topic

Block Time Remaining: 00:22:26

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Feedback



Suspend



End Block





A 45-year-old woman comes to the office for progressive itchininess and fatigue. She also notes yellowing of the eyes and skin. Physical examination shows scleral icterus, multiple excoriations on both the upper and the lower extremities, and hepatomegaly. Laboratory results are as follows:

Liver function studies

Total bilirubin	5.3 mg/dL
Alkaline phosphatase	982 U/L
Aspartate aminotransferase (SGOT)	89 U/L
Alanine aminotransferase (SGPT)	67 U/L
Gamma-glutamyl transpeptidase	450 U/L

Liver biopsy reveals dense lymphocytic infiltration of the portal triads, as well as granulomatous destruction of intralobular bile ducts. Which of the following is the most likely diagnosis?

- ☐ A. Acute hepatitis B
- ☐ B. Autoimmune hepatitis





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Alkaline phosphatase 982 U/L

Aspartate aminotransferase (SGOT) 89 U/L

Alanine aminotransferase (SGPT) 67 U/L

Gamma-glutamyl transpeptidase 450 U/L

Liver biopsy reveals dense lymphocytic infiltration of the portal triads, as well as granulomatous destruction of intralobular bile ducts. Which of the following is the most likely diagnosis?

- ☐ A. Acute hepatitis B
- ☐ B. Autoimmune hepatitis
- ☐ C. Primary biliary cholangitis
- ☐ D. Primary sclerosing cholangitis
- ☐ E. Sarcoidosis

**Submit**

Block Time Remaining: 00:22:32

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1



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Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Alkaline phosphatase 982 U/L

Aspartate aminotransferase (SGOT) 89 U/L

Alanine aminotransferase (SGPT) 67 U/L

Gamma-glutamyl transpeptidase 450 U/L

Liver biopsy reveals dense lymphocytic infiltration of the portal triads, as well as granulomatous destruction of intralobular bile ducts. Which of the following is the most likely diagnosis?

- ☐ A. Acute hepatitis B (1%)
- ☐ B. Autoimmune hepatitis (4%)
- ☒ C. Primary biliary cholangitis (75%)
- ☐ D. Primary sclerosing cholangitis (14%)
- ☐ E. Sarcoidosis (3%)



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



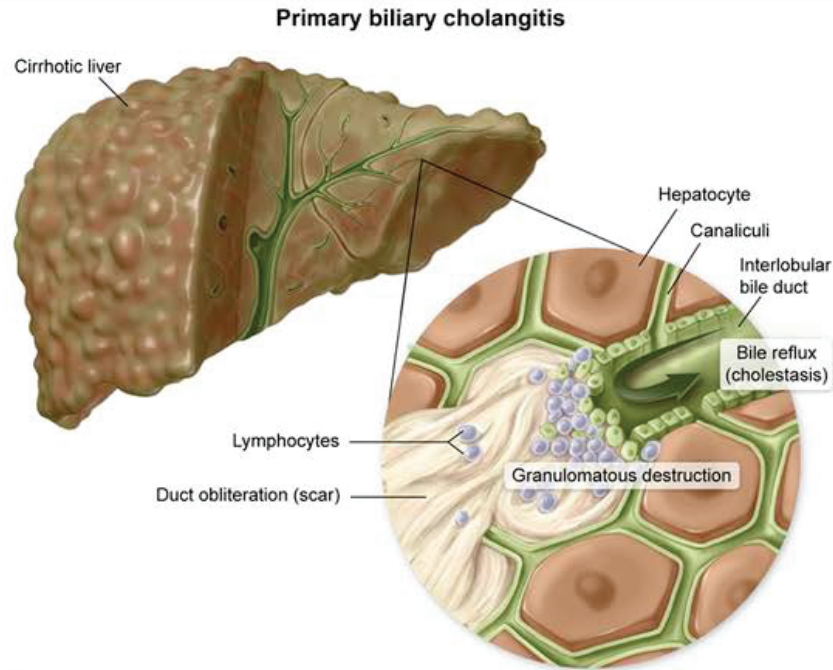
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## Primary biliary cholangitis

### Exhibit Display



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New | Existing



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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This patient with fatigue, pruritus, jaundice, and elevated alkaline phosphatase has liver biopsy results consistent with **primary biliary cholangitis** (PBC), a chronic autoimmune disorder that disproportionately affects **middle-aged women**. PBC is characterized by T-cell-mediated destruction of the small intralobular bile ducts, which is visualized histologically as a **dense lymphocytic inflammation** of portal tracts with **granulomatous destruction of interlobular bile ducts** (ie, florid duct lesions).

PBC typically develops insidiously; **fatigue** and **pruritus** are often the presenting symptoms. **Cholestasis** results in a characteristic pattern of liver injury (ie, **elevated alkaline phosphatase**, elevated gamma-glutamyl transferase, direct hyperbilirubinemia, normal or mildly elevated aminotransferases) and examination findings (eg, hepatomegaly, jaundice). Hypercholesterolemia is also common due to reduced cholesterol excretion. Elevated **antimitochondrial antibodies** are highly characteristic.

**(Choices A and B)** Acute hepatitis B and autoimmune hepatitis (AIH) both result in a **hepatocellular**, not a cholestatic, pattern of liver injury. Hepatitis B is characterized histologically by lobular mononuclear inflammation, hepatocyte balloon degeneration, and ground-glass hepatocytes, whereas AIH results in portal and periportal lymphoplasmacytic infiltration of the liver (ie, interface hepatitis).

**(Choice D)** Primary sclerosing cholangitis causes a cholestatic pattern of liver injury but it is identified



1



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

## Exhibit Display

This patient with features  
consistent with primary biliary  
cholestasis affects middle-aged  
women, which is  
characteristic of  
**granulomatous** disease.

PBC typically develops  
results in a characteristic  
glutamyl transferase  
examination finding  
cholesterol excretion

(Choices A and B) are  
cholestatic, pattern  
inflammation, hepatic  
portal and periportal

(Choice D) Primary

Patterns of liver injury	
Hepatocellular	Cholestatic
<ul style="list-style-type: none"><li>• AST &amp; ALT &gt;&gt; alkaline phosphatase</li><li>• ↑ Bilirubin</li></ul>	<ul style="list-style-type: none"><li>• Alkaline phosphatase &gt;&gt; AST &amp; ALT</li><li>• ↑ Bilirubin</li><li>• ↑ Gamma-glutamyl transferase</li></ul>

AST = aspartate transaminase; ALT = alanine aminotransferase.

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Block Time Remaining: 00:23:26

<https://t.me/USMLEWorldStep1>



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

portal and periportal lymphoplasmacytic infiltration of the liver (ie, interface hepatitis).

**(Choice D)** Primary sclerosing cholangitis causes a cholestatic pattern of liver injury but it is identified histologically by fibrous obliteration of bile ducts, as well as concentric periductal deposition of connective tissue in an onion skin–like pattern. It is strongly associated with ulcerative colitis.

**(Choice E)** Sarcoidosis can cause a cholestatic pattern of liver injury but is characterized by **noncaseating granulomas** with hepatic fibrosis and a multinucleated giant cell formation. The dense portal lymphocytic infiltration characteristic of PBC is not seen. In addition, most patients have symptoms of systemic sarcoidosis (eg, cough, hilar lymphadenopathy).

### Educational objective:

Primary biliary cholangitis is an autoimmune disorder that most commonly affects middle-aged women and is characterized by fatigue, pruritus, jaundice, cholestasis (eg, elevated alkaline phosphatase, elevated gamma-glutamyl transferase, direct hyperbilirubinemia), and antimitochondrial antibodies. Histologic findings include dense lymphocytic portal tract inflammation with granulomatous destruction of interlobular bile ducts (ie, florid duct lesions).

### References

- [Primary biliary cirrhosis: pathophysiology, clinical presentation and therapy](#)

Block Time Remaining: 00:23:26

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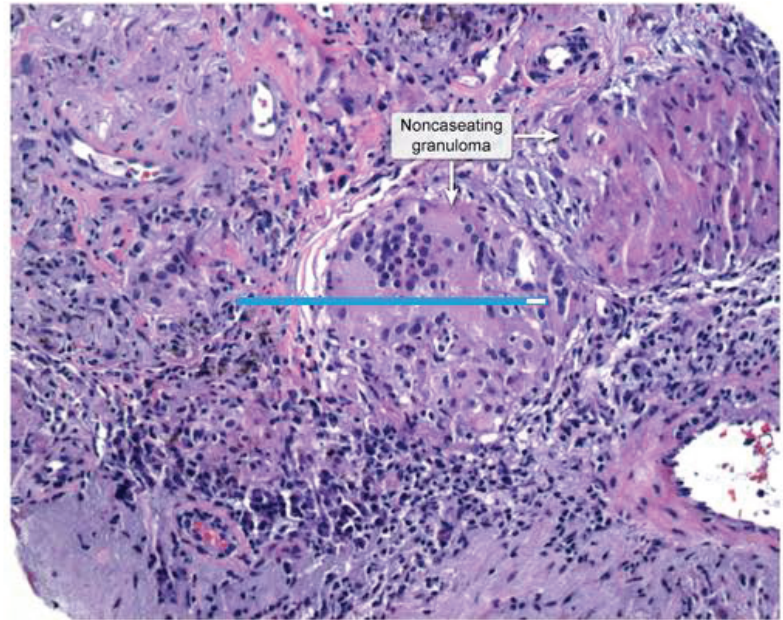
Feedback

Suspend

End Block

Exhibit Display

Noncaseating granuloma



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Primary biliary cirrhosis: pathophysiology, clinical presentation and therapy

Block Time Remaining: 00:23:26

<https://t.me/USMLEWorldStep1>





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 65-year-old man comes to the emergency department due to abdominal pain and diarrhea. Three weeks ago, he drove from Texas to Mexico for a family vacation. Temperature is 38.3 C (101 F), blood pressure is 115/70 mm Hg, and pulse is 98/min. Abdominal examination shows mild, generalized tenderness with no rebound tenderness or guarding. Leukocyte count is 14,000/mm<sup>3</sup>. Sigmoidoscopy demonstrates white-yellow plaques on the colonic mucosa, and biopsy shows that the plaques are composed of fibrin and inflammatory cells. Further questioning regarding this patient's trip to Mexico is most likely to reveal which of the following events?

- ☐ A. He consumed shellfish from the hotel buffet
- ☐ B. He drank unpurified tap water on several occasions
- ☐ C. He had undercooked pork at a resort barbecue
- ☐ D. He required hospitalization and antibiotics for pneumonia
- ☐ E. He took home-canned foods to consume during the trip

**Submit**

Block Time Remaining: 00:23:28

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Feedback



Suspend



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A 65-year-old man comes to the emergency department due to abdominal pain and diarrhea. Three weeks ago, he drove from Texas to Mexico for a family vacation. Temperature is 38.3 C (101 F), blood pressure is 115/70 mm Hg, and pulse is 98/min. Abdominal examination shows mild, generalized tenderness with no rebound tenderness or guarding. Leukocyte count is 14,000/mm<sup>3</sup>. Sigmoidoscopy demonstrates white-yellow plaques on the colonic mucosa, and biopsy shows that the plaques are composed of fibrin and inflammatory cells. Further questioning regarding this patient's trip to Mexico is most likely to reveal which of the following events?

- ☐ A. He consumed shellfish from the hotel buffet (4%)
- ☐ B. He drank unpurified tap water on several occasions (14%)
- ☐ C. He had undercooked pork at a resort barbecue (6%)
- ☒ D. He required hospitalization and antibiotics for pneumonia (74%)
- ☐ E. He took home-canned foods to consume during the trip (1%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### ***Clostridium difficile* colitis**

#### **Risk factors**

- Recent antibiotics
- Hospitalization
- PPI

#### **Pathogenesis**

- Disruption of intestinal flora → *C difficile* overgrowth
- Exotoxins cause mucosal injury
- Pseudomembrane formation

#### **Clinical presentation**

- Profuse diarrhea (most common)
- Fulminant colitis/toxic megacolon

- PCR for toxin-encoding gene



1



Feedback



Suspend



End Block



Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**Pathogenesis**

- Disruption of intestinal flora → *C difficile* overgrowth
- Exotoxins cause mucosal injury
- Pseudomembrane formation

**Clinical presentation**

- Profuse diarrhea (most common)
- Fulminant colitis/toxic megacolon

**Diagnosis**

- PCR for toxin-encoding gene
- EIA for bacterial toxin or glutamate dehydrogenase

**Treatment**

- Oral vancomycin or fidaxomicin

**EIA** = enzyme immunoassay; **PCR** = polymerase chain reaction; **PPI** = proton pump inhibitor.

Block Time Remaining: 00:24:04

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reaction; **PPI** = proton pump inhibitor.

This patient has abdominal pain, diarrhea, and leukocytosis. The formation of **pseudomembranes** (white-yellow plaques composed of fibrin, inflammatory cells, and cellular debris) on the colonic mucosa is highly consistent with pseudomembranous colitis due to ***Clostridium difficile***, a spore-forming bacillus that colonizes up to 50% of hospitalized adults. **Antibiotic therapy** (eg, fluoroquinolones for bacterial pneumonia) **increases the risk** of *C difficile* infection as it kills intestinal microbes that normally keep potential pathogens in check. *C difficile* can proliferate in the altered microbiome, leading to overgrowth and clinical disease.

*C difficile* produces 2 toxins—toxin A (enterotoxin) and toxin B (cytotoxin)—which penetrate colonic epithelial cells and damage cellular cytoskeletons and intercellular tight junctions. This results in widespread inflammation, edema, necrosis, and fibrin deposition. Clinical manifestations range from watery diarrhea and mild abdominal cramping to fulminant colitis with nonobstructive colonic enlargement (megacolon) and intestinal perforation.

**(Choices A and B)** Ingestion of undercooked shellfish is associated with *Vibrio*, Norwalk virus, and hepatitis A infections. Traveler's diarrhea, caused by bacteria (eg, enterotoxigenic *Escherichia coli*, *Campylobacter*, *Salmonella*, *Shigella*) or parasites (eg, *Giardia*), is often due to contaminated water





Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choices A and B) Ingestion of undercooked shellfish is associated with *Vibrio*, Norwalk virus, and hepatitis A infections. Traveler's diarrhea, caused by bacteria (eg, enterotoxigenic *Escherichia coli*, *Campylobacter*, *Salmonella*, *Shigella*) or parasites (eg, *Giardia*), is often due to contaminated water consumption. These conditions can manifest as diarrhea and abdominal pain; however, pseudomembranes are virtually pathognomonic for *C difficile* colitis.

(Choice C) Consumption of undercooked pork is a risk factor for intestinal tapeworm (taeniasis), which occurs after ingestion of *Taenia solium*. Patients are often asymptomatic but may have nausea or abdominal pain.

(Choice E) Adult botulism occurs after ingestion of preformed toxin in home-canned food. This neurotoxin inhibits acetylcholine release from the nerve terminals at neuromuscular junctions and causes a descending flaccid paralysis.

### Educational objective:

Antibiotics disrupt the normal intestinal flora and which can allow for overgrowth of *Clostridium difficile*, an anaerobic, gram-positive, spore-forming bacillus. *C difficile* produces 2 toxins that penetrate colonic epithelial cells leading to watery diarrhea, abdominal cramping, and colitis. The presence of a pseudomembrane (exudate on colonic mucosa consisting of fibrin and inflammatory cells) is highly suggestive of *C difficile* infection.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 6-year-old girl is brought to the office due to intermittent abdominal cramps, bloating, and diarrhea for 2 months. She also has excessive flatulence, which typically occurs after meals. The patient has had no fever or vomiting. She eats a well-balanced diet and takes no medications or vitamins. Vital signs are appropriate for age. Examination shows a mildly distended abdomen with no hepatosplenomegaly or tenderness. Laboratory evaluation reveals elevated tissue transglutaminase antibodies. Which of the following locations should be biopsied to confirm the diagnosis in this patient?

- ☐ A. Stomach
- ☐ B. Duodenum
- ☐ C. Distal jejunum
- ☐ D. Terminal ileum
- ☐ E. Colon

**Submit**

Block Time Remaining: 00:24:05

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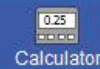
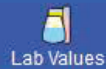


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A 6-year-old girl is brought to the office due to intermittent abdominal cramps, bloating, and diarrhea for 2 months. She also has excessive flatulence, which typically occurs after meals. The patient has had no fever or vomiting. She eats a well-balanced diet and takes no medications or vitamins. Vital signs are appropriate for age. Examination shows a mildly distended abdomen with no hepatosplenomegaly or tenderness. Laboratory evaluation reveals elevated tissue transglutaminase antibodies. Which of the following locations should be biopsied to confirm the diagnosis in this patient?

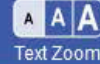
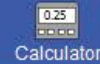
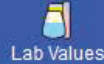
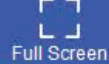
- ☐ A. Stomach (1%)
- ✓ ☒ B. Duodenum (63%)
- ☐ C. Distal jejunum (17%)
- ☐ D. Terminal ileum (15%)
- ☐ E. Colon (2%)

Correct

 63%  
Answered correctly 52 secs  
Time Spent 10/06/2020  
Last Updated

Block Time Remaining: 00:24:56

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### Celiac disease

<b>Pathogenesis</b>	<ul style="list-style-type: none"><li>• Gluten (gliadin) consumption → immune-mediated small intestine inflammation → chronic malabsorption</li></ul>
<b>Symptoms</b>	<ul style="list-style-type: none"><li>• Abdominal pain</li><li>• Diarrhea, flatulence &amp; bloating</li><li>• Failure to thrive (children) or weight loss</li><li>• Iron deficiency anemia</li><li>• Dermatitis herpetiformis</li></ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"><li>• Serology: tissue transglutaminase IgA, antiendomysial antibodies</li><li>• Duodenal biopsy: intraepithelial lymphocytes, villous atrophy, crypt hyperplasia</li></ul>
<b>Associated conditions</b>	<ul style="list-style-type: none"><li>• Autoimmune disorders (eg, type 1 diabetes)</li><li>• Cancer risk: T-cell lymphoma</li></ul>

This patient with chronic gastrointestinal symptoms and elevated **tissue transglutaminase (TTG) antibodies** likely has **celiac disease**. This chronic, malabsorptive disorder is caused by an immune-





Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient with chronic gastrointestinal symptoms and elevated **tissue transglutaminase (TTG) antibodies** likely has **celiac disease**. This chronic, malabsorptive disorder is caused by an immune-mediated reaction to dietary gliadin (the major component of **gluten**) found in wheat, barley, and rye.

In patients with celiac disease, gliadin triggers an **inflammatory reaction** within the small intestine that leads to the classic symptoms of abdominal pain, distension, flatulence, and diarrhea. Laboratory evaluation usually reveals antibodies against TTG, a crosslinking enzyme that interacts with glutamine-rich proteins (including exogenous gliadin). Endoscopy with biopsy characteristically shows villus atrophy, lymphocytic infiltration of the intraepithelial cells, and crypt hyperplasia. Biopsy of the **duodenum** and **proximal jejunum** are most likely to confirm the diagnosis because these areas of the intestine are exposed to the **highest concentration of gliadin**.

**(Choice A)** *Helicobacter pylori* infection, which predisposes to gastritis and peptic ulcer disease, can cause abdominal pain (often postprandial) and bloating, and gastric biopsy can confirm the diagnosis. However, elevated TTG antibodies are not associated with *H pylori*.

**(Choices C, D, and E)** Because celiac disease primarily involves the proximal small bowel, biopsies from the distal jejunum and terminal ileum may be normal in patients with celiac disease and are not







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

evaluation usually reveals antibodies against TTG, a crosslinking enzyme that interacts with glutamine-rich proteins (including exogenous gliadin). Endoscopy with biopsy characteristically shows villus atrophy, lymphocytic infiltration of the intraepithelial cells, and crypt hyperplasia. Biopsy of the **duodenum** and **proximal jejunum** are most likely to confirm the diagnosis because these areas of the intestine are exposed to the **highest concentration of gliadin**.

**(Choice A)** *Helicobacter pylori* infection, which predisposes to gastritis and peptic ulcer disease, can cause abdominal pain (often postprandial) and bloating, and gastric biopsy can confirm the diagnosis. However, elevated TTG antibodies are not associated with *H pylori*.

**(Choices C, D, and E)** Because celiac disease primarily involves the proximal small bowel, biopsies from the distal jejunum and terminal ileum may be normal in patients with celiac disease and are not recommended; the colon is not affected in celiac disease.

### Educational objective:

Celiac disease is caused by an immune-mediated reaction to gluten and classically leads to chronic gastrointestinal symptoms. Diagnosis is confirmed by elevated tissue transglutaminase IgA antibody levels and duodenal biopsy showing villus flattening, intraepithelial lymphocyte infiltration, and crypt hyperplasia.



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



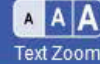
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 60-year-old woman comes to the office with intermittent flatulence, crampy abdominal pain, and watery diarrhea. Her symptoms started 2 months ago after she recovered from an episode of acute gastroenteritis associated with nausea, vomiting, and diarrhea. The patient's symptoms are worse after drinking "too much milk." She usually has 1 or 2 glasses of wine every evening with dinner. Physical examination is unremarkable. Initial laboratory evaluation, including serum chemistries, blood counts, stool cultures, and studies for ova and parasites, is negative. Which of the following is most likely decreased in this patient?

- ☐ A. Breath hydrogen content
- ☐ B. Fecal fat
- ☐ C. Pancreatic enzymes
- ☐ D. Stool osmolality
- ☐ E. Stool pH

**Submit**

Block Time Remaining: 00:24:57

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 60-year-old woman comes to the office with intermittent flatulence, crampy abdominal pain, and watery diarrhea. Her symptoms started 2 months ago after she recovered from an episode of acute gastroenteritis associated with nausea, vomiting, and diarrhea. The patient's symptoms are worse after drinking "too much milk." She usually has 1 or 2 glasses of wine every evening with dinner. Physical examination is unremarkable. Initial laboratory evaluation, including serum chemistries, blood counts, stool cultures, and studies for ova and parasites, is negative. Which of the following is most likely decreased in this patient?

- ☐ A. Breath hydrogen content (9%)
- ☐ B. Fecal fat (2%)
- ☐ C. Pancreatic enzymes (17%)
- ☐ D. Stool osmolality (23%)
- ☒ E. Stool pH (47%)

Correct

 47%  
Answered correctly 23 secs  
Time Spent 08/25/2020  
Last Updated

Block Time Remaining: 00:25:19

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient's presentation with flatulence, crampy abdominal pain, and watery diarrhea after consuming dairy products (eg, milk) is consistent with **lactose intolerance**. The most common cause of lactose intolerance is lactase nonpersistence, which is especially prevalent in Asian and African populations and is characterized by declining lactase expression in adulthood. This patient's lactose intolerance is most likely due to **secondary lactase deficiency**, an acquired condition resulting from inflammation/infection (eg, bacterial overgrowth, **infectious enteritis**, Crohn disease) that causes injury to the mucosal brush border of the small bowel where lactase is expressed.

Lactase deficiency results in incomplete hydrolysis of lactose into the monosaccharides glucose and galactose. The fermentation of undigested lactose by gut bacteria leads to increased production of short-chain fatty acids (eg, acetate, butyrate, propionate) that acidify the stool (**decreased stool pH**). During this process, hydrogen gas is also produced, leading to **increased breath hydrogen content (Choice A)**. In addition, the high amounts of undigested lactose in the bowel lead to **elevated stool osmolality**, which attracts excess water in the bowel lumen, causing osmotic diarrhea (**Choice D**).

**(Choice B)** Inflammation/infection of the small intestine may lead to fat malabsorption, resulting in steatorrhea (eg, greasy, malodorous stool that is difficult to flush), weight loss, and increased fecal fat content. Fat malabsorption does not typically occur in patients with lactase deficiency.



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

process, hydrogen gas is also produced, leading to **increased breath hydrogen content (Choice A)**. In addition, the high amounts of undigested lactose in the bowel lead to **elevated stool osmolality**, which attracts excess water in the bowel lumen, causing osmotic diarrhea **(Choice D)**.

**(Choice B)** Inflammation/infection of the small intestine may lead to fat malabsorption, resulting in steatorrhea (eg, greasy, malodorous stool that is difficult to flush), weight loss, and increased fecal fat content. Fat malabsorption does not typically occur in patients with lactase deficiency.

**(Choice C)** Reduced pancreatic enzyme production (exocrine insufficiency) can occur with chronic pancreatitis, which is seen frequently in individuals with chronic alcoholism. Pancreatic enzyme levels are not affected by secondary lactase deficiency.

### Educational objective:

Lactose intolerance presents with flatulence, crampy abdominal pain, and watery diarrhea after dairy product consumption. It can be acquired by inflammatory/infectious conditions that injure the mucosal brush border of the small intestine where lactase is expressed. Studies can show increased breath hydrogen content, reduced stool pH, and elevated stool osmolality.

### References

- [Lactose intolerance in adults: biological mechanism and dietary management.](#)



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 45-year-old woman recently diagnosed with Sjögren's syndrome complains of severe pruritus that slowly progressed over the last year. She says that pruritus is especially prominent over palms and soles and is unbearable during the night. Laboratory testing shows:

Total bilirubin	1.0 mg/dL
Direct bilirubin	0.8 mg/dL
Alkaline phosphatase	720 U/L
Aspartate aminotransferase (SGOT)	48 U/L
Alanine aminotransferase (SGPT)	40 U/L

This patient most likely has which of the following conditions?

A. Viral hepatitis B

Block Time Remaining: 00:25:20

<https://t.me/USMLEWorldStep1>



Feedback

Suspend

End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Aspartate aminotransferase

48 U/L

(SGOT)

Alanine aminotransferase

40 U/L

(SGPT)

This patient most likely has which of the following conditions?

- ☐ A. Viral hepatitis B
- ☐ B. Viral hepatitis C
- ☐ C. Alcoholic hepatitis
- ☐ D. Budd-Chiari syndrome
- ☐ E. Primary biliary cholangitis
- ☐ F. Hemochromatosis
- ☐ G. Wilson's disease

Block Time Remaining: 00:25:23

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Alanine aminotransferase  
(SGPT)

40 U/L

This patient most likely has which of the following conditions?

- ☐ A. Viral hepatitis B (0%)
- ☐ B. Viral hepatitis C (0%)
- ☐ C. Alcoholic hepatitis (2%)
- ☐ D. Budd-Chiari syndrome (3%)
- ☒ E. Primary biliary cholangitis (90%)
- ☐ F. Hemochromatosis (1%)
- ☐ G. Wilson's disease (0%)

Correct

 90%  
Answered correctly01 min, 03 secs  
Time Spent10/04/2020  
Last Updated

Block Time Remaining: 00:26:22

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



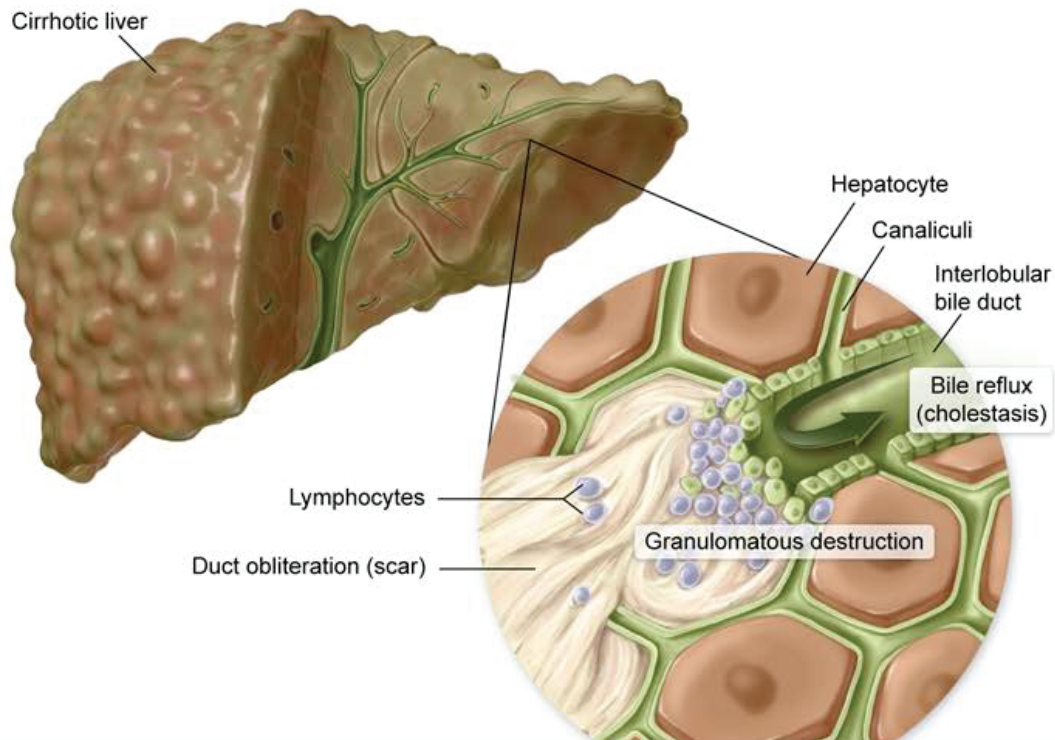
Text Zoom



Settings

## Primary biliary cholangitis

Cirrhotic liver



Hepatocyte

Canaliculi

Interlobular  
bile ductBile reflux  
(cholestasis)

Lymphocytes

Granulomatous destruction

Duct obliteration (scar)



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient is suffering from **primary biliary cholangitis** (PBC), a chronic liver disease characterized by autoimmune destruction of the intrahepatic bile ducts and cholestasis. The condition presents most commonly in **middle-aged women** and is insidious in onset. **Pruritus** is usually the first symptom and may be very severe, especially at night. Fatigue is also often reported. Physical findings typically include hepatosplenomegaly and xanthomatous lesions in the eyelids or in the skin and tendons. As the disease progresses, jaundice, steatorrhea, and portal hypertension may develop.

Abnormalities on laboratory testing are consistent with cholestasis and include **elevated alkaline phosphatase** cholesterol, and bile acids (causing pruritus) due to spillage of bile into the blood. Diagnosis is confirmed with demonstration of **anti-mitochondrial antibodies** in the serum. Associated conditions include **autoimmune diseases** such as Sjögren's syndrome, Raynaud's syndrome, systemic sclerosis, and Hashimoto's thyroiditis.

**(Choices A and B)** Expected laboratory findings in a patient with acute viral hepatitis include significant elevations in ALT and AST (with ALT > AST), followed by rises in bilirubin.

**(Choice C)** Alcoholic hepatitis is typically associated with a significant drinking history and is commonly characterized by an AST:ALT ratio greater than 2:1.

**(Choice D)** Budd-Chiari syndrome arises secondary to thrombotic occlusion of the hepatic veins and/or





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Hashimoto's thyroiditis.

**(Choices A and B)** Expected laboratory findings in a patient with acute viral hepatitis include significant elevations in ALT and AST (with ALT > AST), followed by rises in bilirubin.

**(Choice C)** Alcoholic hepatitis is typically associated with a significant drinking history and is commonly characterized by an AST:ALT ratio greater than 2:1.

**(Choice D)** Budd-Chiari syndrome arises secondary to thrombotic occlusion of the hepatic veins and/or the intra- or suprahepatic inferior vena cava. The venous occlusion causes the sinusoidal pressure to increase, ultimately leading to portal hypertension, ascites, hepatomegaly, and splenomegaly.

**(Choices F and G)** Hemochromatosis and Wilson's disease cause hepatocellular injury and thus are associated with elevated ALT and AST rather than cholestatic picture.

**Educational objective:**

Primary biliary cholangitis is a chronic liver disease characterized by autoimmune destruction of the intrahepatic bile ducts and cholestasis (elevated alkaline phosphatase). The condition is most common in middle-aged women, with severe pruritus (especially at night) often one of the first reported symptoms.



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Feedback



Suspend



End Block

A 38-year-old woman comes to the office due to jaundice, nausea, and abdominal discomfort. Vital signs are within normal limits. Scleral icterus and hepatomegaly are present. Laboratory results are as follows:

Liver function studies

Total bilirubin	4.7 mg/dL
Alkaline phosphatase	110 U/L
Aspartate aminotransferase (SGOT)	791 U/L
Alanine aminotransferase (SGPT)	634 U/L

Anti-smooth muscle antibody titers are elevated. Which of the following histologic findings is most likely to be seen on biopsy of this patient's liver?

- ☐ A. Ground-glass hepatocytes with central ballooning degeneration
- ☐ B. Hepatic steatosis and ballooning degeneration
- ☐ C. Hepatocyte necrosis with portal infiltration of neutrophils
- ☐ D. Periductal fibrosis and luminal obliteration of biliary ducts





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Total bilirubin	4.7 mg/dL
Alkaline phosphatase	110 U/L
Aspartate aminotransferase (SGOT)	791 U/L
Alanine aminotransferase (SGPT)	634 U/L

Anti-smooth muscle antibody titers are elevated. Which of the following histologic findings is most likely to be seen on biopsy of this patient's liver?

- ☐ A. Ground-glass hepatocytes with central ballooning degeneration
- ☐ B. Hepatic steatosis and ballooning degeneration
- ☐ C. Hepatocyte necrosis with portal infiltration of neutrophils
- ☐ D. Periductal fibrosis and luminal obliteration of biliary ducts
- ☐ E. Portal and periportal lymphoplasmacytic cell infiltration

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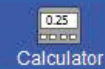
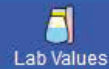
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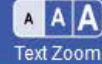
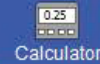
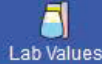
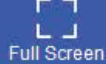


Total bilirubin	4.7 mg/dL
Alkaline phosphatase	110 U/L
Aspartate aminotransferase (SGOT)	791 U/L
Alanine aminotransferase (SGPT)	634 U/L

Anti-smooth muscle antibody titers are elevated. Which of the following histologic findings is most likely to be seen on biopsy of this patient's liver?

- ☐ A. Ground-glass hepatocytes with central ballooning degeneration (5%)
- ☐ B. Hepatic steatosis and ballooning degeneration (6%)
- ☐ C. Hepatocyte necrosis with portal infiltration of neutrophils (9%)
- ☐ D. Periductal fibrosis and luminal obliteration of biliary ducts (35%)
- ☒ E. Portal and periportal lymphoplasmacytic cell infiltration (41%)





This patient with jaundice, hepatomegaly, elevated transaminases, and high anti-smooth muscle antibody titers most likely has **autoimmune hepatitis** (AIH). AIH occurs most commonly in women with other autoimmune conditions (eg, type 1 diabetes mellitus). It is often asymptomatic but may present with fatigue, weight loss, nausea, and/or signs of acute hepatitis (eg, jaundice, abdominal discomfort).

Characteristic laboratory abnormalities include a **hepatocellular pattern** of liver injury (ie, predominant transaminase elevation with normal alkaline phosphatase and variable bilirubin) and the formation of a variety of autoantibodies, particularly **anti-smooth muscle**, which is highly specific for AIH.

Hypergammaglobulinemia is also typical.

The pathogenesis of AIH is incompletely understood but likely involves exposure to an environmental trigger in genetically predisposed patients, leading to regulatory T-cell dysfunction. It ultimately results in loss of self-tolerance, with an **immune response against hepatic antigens**. This is demonstrated histologically by **lymphocyte and plasma cell** infiltration of **portal and periportal** regions of the liver.

**(Choice A)** Chronic hepatitis B is characterized histologically by ground-glass hepatocytes, which result from the accumulation of hepatitis B surface antigen within their cytoplasm, as well as central balloon degeneration, which reflects hepatocytes undergoing apoptosis.







histologically by **lymphocyte and plasma cell** infiltration of **portal and periportal** regions of the liver.

**(Choice A)** Chronic hepatitis B is characterized histologically by ground-glass hepatocytes, which result from the accumulation of hepatitis B surface antigen within their cytoplasm, as well as central balloon degeneration, which reflects hepatocytes undergoing apoptosis.

**(Choice B)** Hepatic steatosis (ie, lipid accumulation in the cytoplasm of hepatocytes) and ballooning degeneration most commonly occur in alcoholic hepatitis and nonalcoholic fatty liver disease. Elevated anti-smooth muscle antibody titers do not occur.

**(Choice C)** Acetaminophen overdose can lead to hepatic inflammation and necrosis with neutrophilic infiltration (unlike AIH, which is characterized by lymphoplasmacytic infiltrates). Patients often have vomiting, diaphoresis, and confusion.

**(Choice D)** Primary sclerosing cholangitis causes periductal fibrosis and luminal obliteration of the biliary ducts, which can lead to cholestasis. High alkaline phosphatase levels and near-normal aminotransferases are expected.

### Educational objective:

Autoimmune hepatitis results from an immune response against hepatic antigens, leading to a lymphoplasmacytic infiltrate in the portal and periportal regions of the liver. Manifestations include fatigue,





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice B)** Hepatic steatosis (ie, lipid accumulation in the cytoplasm of hepatocytes) and ballooning degeneration most commonly occur in alcoholic hepatitis and nonalcoholic fatty liver disease. Elevated anti-smooth muscle antibody titers do not occur.

**(Choice C)** Acetaminophen overdose can lead to hepatic inflammation and necrosis with neutrophilic infiltration (unlike AIH, which is characterized by lymphoplasmocytic infiltrates). Patients often have vomiting, diaphoresis, and confusion.

**(Choice D)** Primary sclerosing cholangitis causes periductal fibrosis and luminal obliteration of the biliary ducts, which can lead to cholestasis. High alkaline phosphatase levels and near-normal aminotransferases are expected.

**Educational objective:**

Autoimmune hepatitis results from an immune response against hepatic antigens, leading to a lymphoplasmacytic infiltrate in the portal and periportal regions of the liver. Manifestations include fatigue, weight loss, nausea, and/or signs of acute hepatitis (eg, jaundice, abdominal discomfort). Characteristic laboratory abnormalities include a hepatocellular pattern of liver injury, anti-smooth muscle autoantibodies, and hypergammaglobulinemia.



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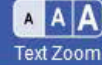
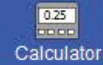
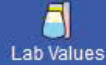
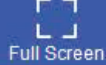
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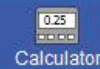
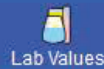


A 25-year-old woman comes to the office due to progressive fatigue and dizziness for several months. She also has intermittent loose stools and abdominal cramps but no hematochezia, melena, vomiting, or abnormal menses. Vital signs are within normal limits. Conjunctival pallor is present. The abdomen is mildly distended but nontender. Laboratory evaluation reveals **anemia** and a **low ferritin level**. Fecal occult blood testing is negative. An upper endoscopy is performed and reveals no visible abnormalities of the stomach or duodenum, although biopsies of the duodenum are significant for **intraepithelial lymphocytosis**. Which of the following is the most likely cause of this patient's condition?

- ☐ A. ~~Brush border enzyme deficiency~~ (11%)
- ☐ B. ~~*Helicobacter pylori* infection~~ (8%)
- ☒ C. HLA-associated autoimmune disorder (68%)
- ☐ D. Irritable bowel syndrome (9%)
- ☐ E. ~~Nonsteroidal anti-inflammatory drugs~~ (1%)







### Celiac disease

<b>Pathogenesis</b>	<ul style="list-style-type: none"><li>• Gluten (gliadin) consumption → immune-mediated small intestine inflammation → chronic malabsorption</li></ul>
<b>Symptoms</b>	<ul style="list-style-type: none"><li>• Abdominal pain</li><li>• Diarrhea, flatulence &amp; bloating</li><li>• Failure to thrive (children) or weight loss</li><li>• Iron deficiency anemia</li><li>• Dermatitis herpetiformis</li></ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"><li>• Serology: tissue transglutaminase IgA, antiendomysial antibodies</li><li>• Duodenal biopsy: intraepithelial lymphocytes, villous atrophy, crypt hyperplasia</li></ul>
<b>Associated conditions</b>	<ul style="list-style-type: none"><li>• Autoimmune disorders (eg, type 1 diabetes)</li><li>• Cancer risk: T-cell lymphoma</li></ul>

This patient with loose stools and crampy abdominal pain has **celiac disease**, an **autoimmune disorder**





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient with loose stools and crampy abdominal pain has **celiac disease**, an **autoimmune disorder** of the small intestine triggered by dietary gluten. Besides intestinal symptoms, celiac disease commonly causes nutrient malabsorption that leads to weight loss, steatorrhea (ie, greasy, malodorous stools), and **deficiency of iron** (eg, anemia, low serum ferritin) and vitamin D (eg, loss of bone density).

Initial testing for celiac disease typically includes an **anti-tissue transglutaminase IgA** assay. The diagnosis is confirmed with duodenal biopsy. The earliest histologic finding is **intraepithelial lymphocytosis**; crypt hyperplasia and **villous blunting** develop later as the disorder progresses.

Celiac disease occurs almost exclusively (>99%) in individuals with an **HLA-DQ2 or -DQ8** serotype. These variants must be present on antigen-presenting cells for recognition of deamidated gliadin (a breakdown product of gluten) and induction of the T-cell-mediated response.

**(Choice A)** Lactose intolerance is caused by a deficiency in lactase, an enzyme located on the small intestine brush border. Although diarrhea is common, lactose intolerance does not cause iron deficiency anemia or intraepithelial lymphocytosis.

**(Choices B and E)** Both *Helicobacter pylori* and nonsteroidal anti-inflammatory drugs can cause iron deficiency due to chronic upper gastrointestinal blood loss. However, they typically cause **gastritis**, duodenitis, or peptic ulcer disease, none of which was identified during this patient's endoscopy. Diarrhea,



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

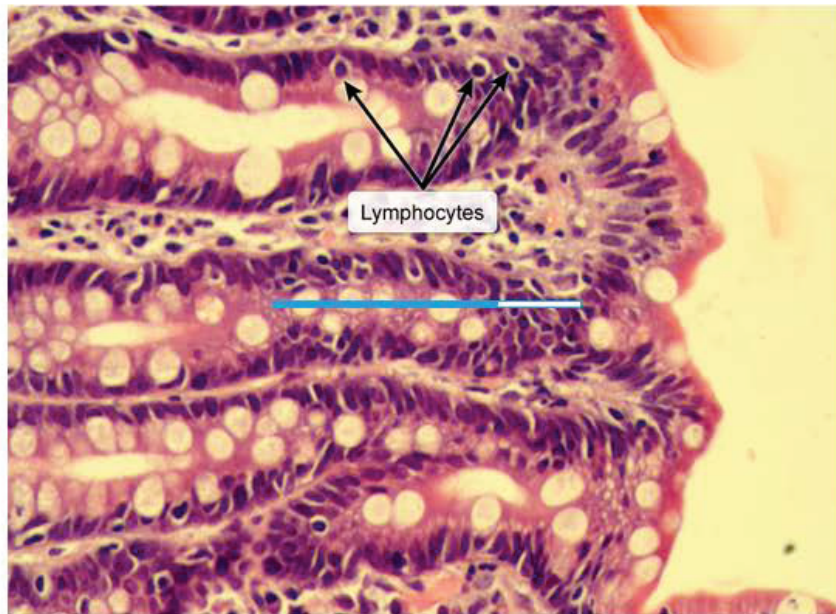
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This patient with loose stools and crampy abdominal pain has **celiac disease**, an autoimmune disorder

## Exhibit Display

## Celiac sprue



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Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:29:39

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Feedback

Suspend

End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

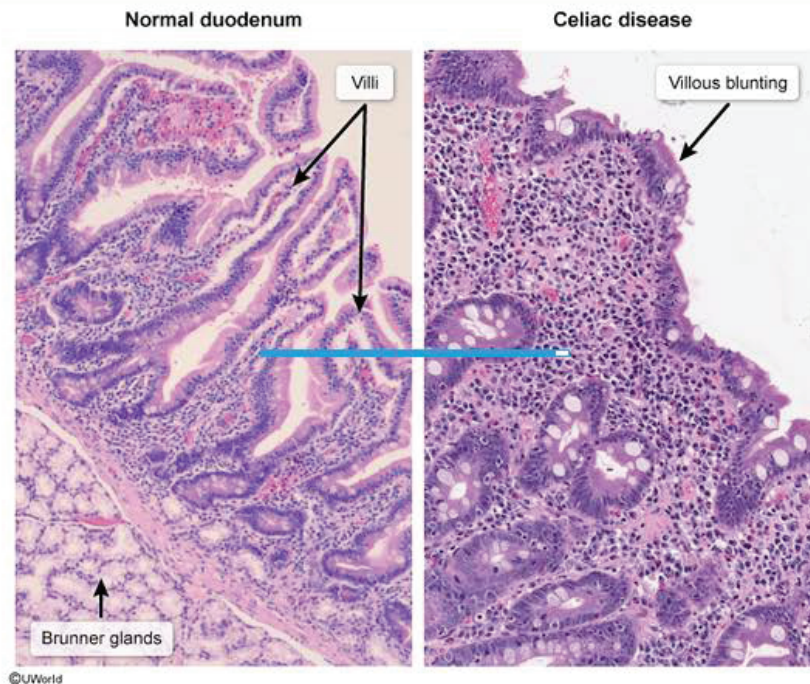
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This patient with loose stools and crampy abdominal pain has **celiac disease**, an autoimmune disorder

## Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:29:39

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Feedback



Suspend

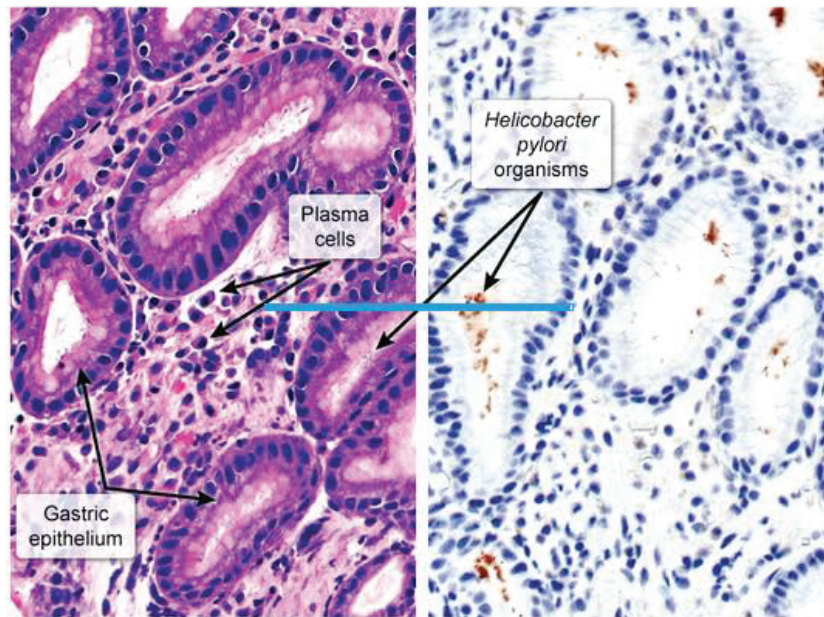


End Block

This patient with loose stools and crampy abdominal pain has **celiac disease**, an autoimmune disorder

## Exhibit Display

## Chronic gastritis



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Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

anemia or intraepithelial lymphocytosis.

**(Choices B and E)** Both *Helicobacter pylori* and nonsteroidal anti-inflammatory drugs can cause iron deficiency due to chronic upper gastrointestinal blood loss. However, they typically cause **gastritis**, duodenitis, or peptic ulcer disease, none of which was identified during this patient's endoscopy. Diarrhea, duodenal lymphocytosis, and a negative fecal occult blood test make celiac disease more likely.

**(Choice D)** Irritable bowel syndrome is a disorder of bowel motility that causes abdominal pain associated with defecation, as well as diarrhea and/or constipation. It does not cause iron deficiency anemia or duodenal intraepithelial lymphocytosis.

### Educational objective:

Celiac disease is an autoimmune disorder triggered by dietary gluten that develops almost exclusively in patients with HLA-DQ2 or -DQ8 serotypes. It often causes diarrhea and malabsorption (eg, iron deficiency anemia). The earliest histologic finding is duodenal intraepithelial lymphocytosis; crypt hyperplasia and villous blunting develop later.

### References

- Intraepithelial lymphocytes, scores, mimickers, and challenges in diagnosing gluten-sensitive enteropathy (celiac disease)



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

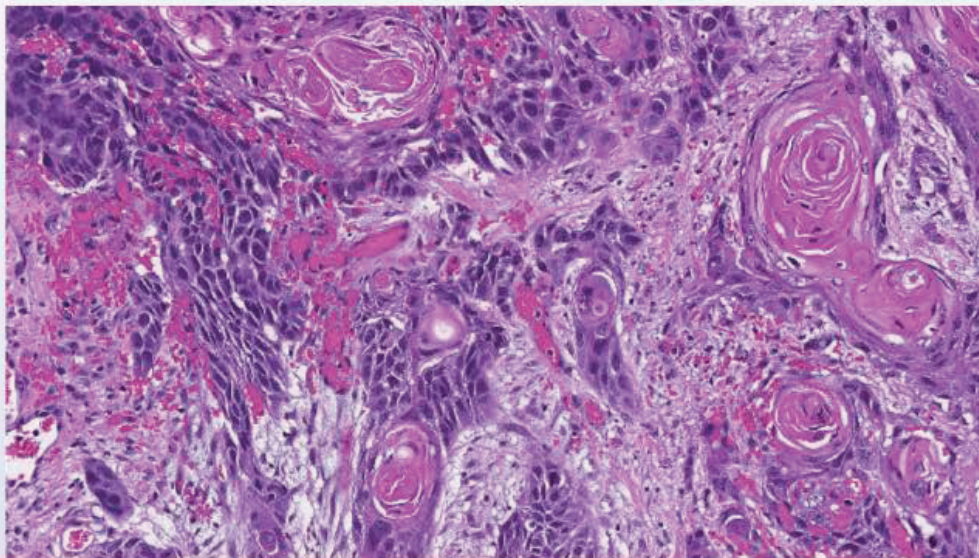


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Settings

A 63-year-old man comes to the office due to several months of dysphagia, fatigue, occasional chest discomfort, and indigestion. He has a history of hypertension and takes amlodipine. The patient smokes 1 or 2 cigars daily. His blood pressure is 140/80 mm Hg. Physical examination is normal. An endoscopic evaluation with esophageal biopsy is performed. The histopathology of the specimen is shown in the image below.



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

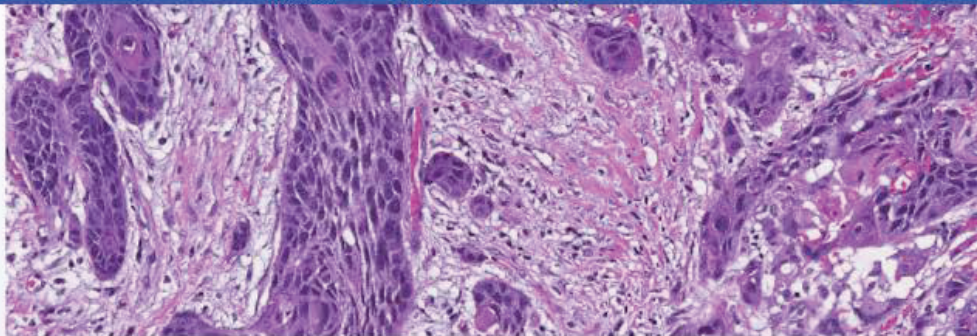
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the most likely cause of this patient's dysphagia?

- ☐ A. Benign tumor with slow growth
- ☐ B. Malignancy with probable poor prognosis
- ☐ C. Metaplasia with increased risk of adenocarcinoma
- ☐ D. Motor dysfunction with increased risk of carcinoma
- ☐ E. Reflux esophagitis with high risk of metaplasia

**Submit**

Block Time Remaining: 00:29:45

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Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

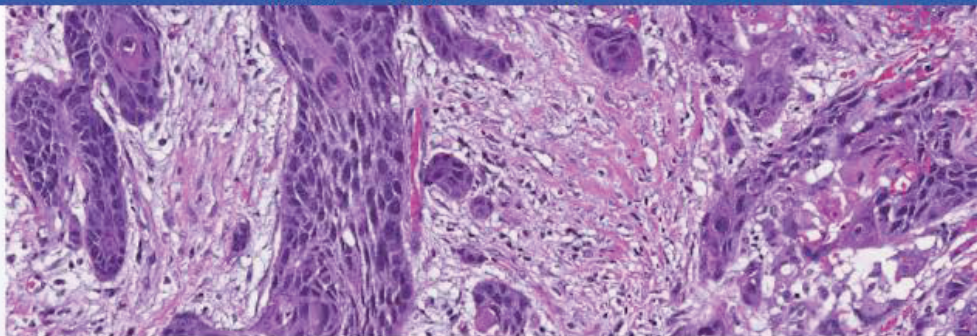
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the most likely cause of this patient's dysphagia?

- ☐ A. Benign tumor with slow growth (1%)
- ☒ B. Malignancy with probable poor prognosis (78%)
- ☐ C. Metaplasia with increased risk of adenocarcinoma (12%)
- ☐ D. Motor dysfunction with increased risk of carcinoma (3%)
- ☐ E. Reflux esophagitis with high risk of metaplasia (3%)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

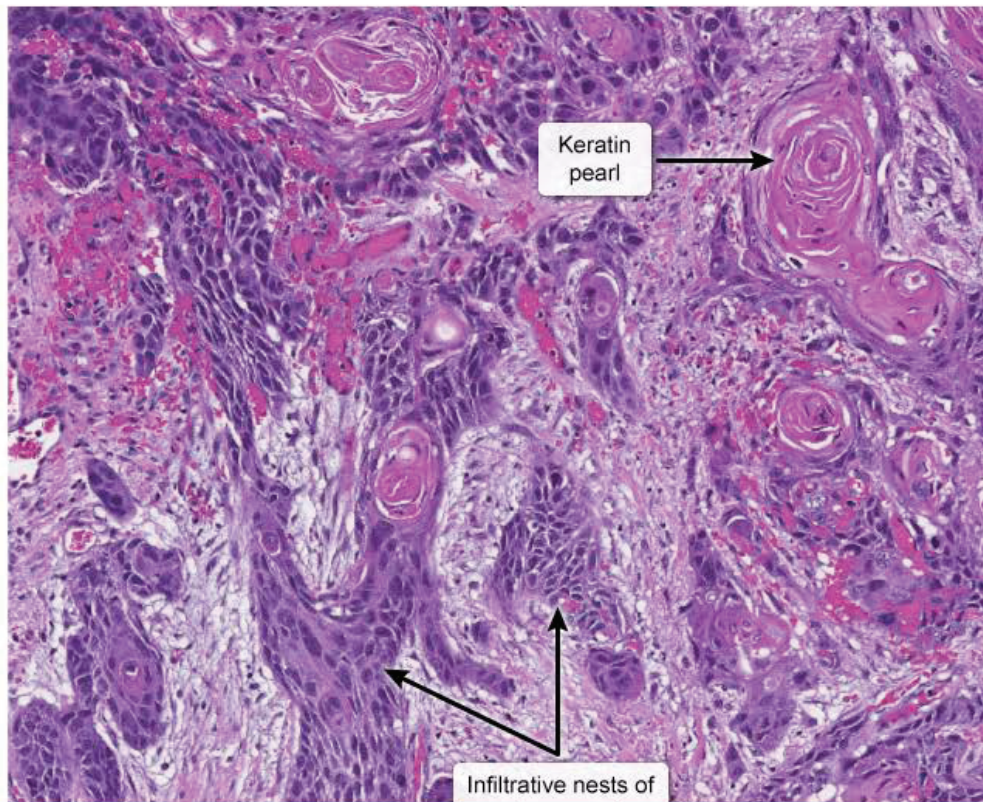


Text Zoom



Settings

## Squamous cell carcinoma



Block Time Remaining: 00:30:37

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient's biopsy is consistent with **esophageal squamous cell carcinoma** (SCC). The histopathologic features of this condition include solid nests of neoplastic squamous cells with abundant eosinophilic cytoplasm and distinct borders (compared to **normal esophagus**). Areas of **keratinization** are identified (keratin pearls). The presence of intercellular bridges is also characteristic of squamous differentiation.

Most cases of esophageal SCC occur in men age >50 with a history of prolonged smoking and alcohol use. Patients typically present with solid food **dysphagia** as the tumor gradually obstructs the esophageal lumen, which can progress to liquid dysphagia. Retrosternal discomfort/burning and significant **weight loss** are also common. Chronic gastrointestinal blood loss may result in iron deficiency anemia with fatigue. The **prognosis** for esophageal cancer is **generally poor** as many patients present with incurable locally advanced or metastatic disease.

**(Choice A)** Benign tumors of the esophagus (most commonly leiomyomas) are rare and slow growing. On light microscopy, **leiomyomas** consist of fascicles of spindle cells with variable amounts of fibrosis.

**(Choices C and E)** **Reflux esophagitis** commonly occurs due to gastroesophageal reflux disease and is characterized histologically by elongation of the papillae, basal cell hyperplasia, and intraepithelial eosinophils. Repeated epithelial injury caused by reflux esophagitis may lead to **Barrett esophagus**, which







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** Benign tumors of the esophagus (most commonly leiomyomas) are rare and slow growing. On light microscopy, **leiomyomas** consist of fascicles of spindle cells with variable amounts of fibrosis.

**(Choices C and E)** **Reflux esophagitis** commonly occurs due to gastroesophageal reflux disease and is characterized histologically by elongation of the papillae, basal cell hyperplasia, and intraepithelial eosinophils. Repeated epithelial injury caused by reflux esophagitis may lead to **Barrett esophagus**, which is characterized by intestinal metaplasia with goblet cells. Barrett esophagus is a premalignant condition that significantly increases the risk of esophageal adenocarcinoma.

**(Choice D)** Achalasia is an esophageal motility disorder characterized by failed relaxation of the lower esophageal sphincter resulting in food retention, dilation of the esophageal body, and symptoms of solid/liquid dysphagia. Achalasia increases the risk of squamous cell carcinoma of the esophagus.

### Educational objective:

The histopathologic features of esophageal squamous cell carcinoma include solid nests of neoplastic squamous cells with abundant eosinophilic cytoplasm and distinct borders. Areas of keratinization and the presence of intercellular bridges are also characteristic. Patients typically present with progressive solid and eventually liquid dysphagia and weight loss.







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

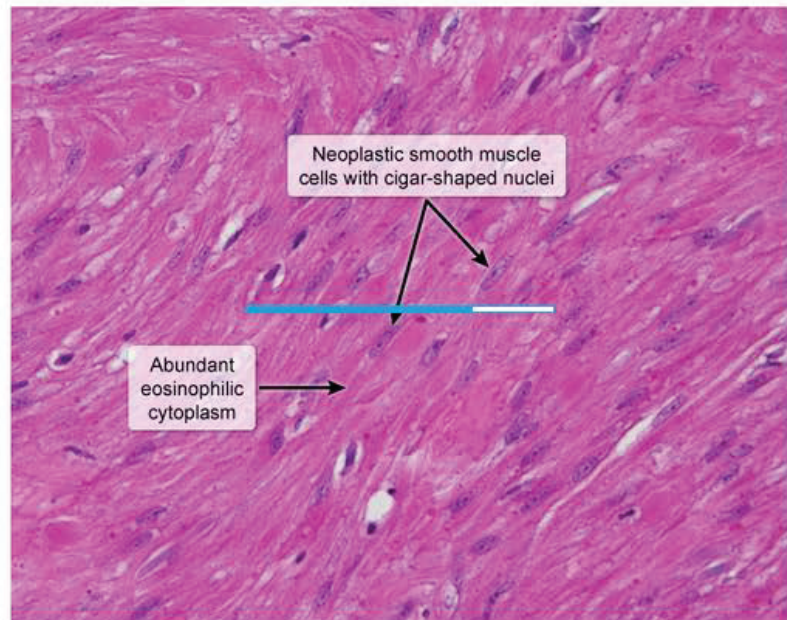
Text Zoom

Settings

(Choice A) Benign tumors of the esophagus (most commonly leiomyomas) are rare and slow-growing. On

## Exhibit Display

## Leiomyoma



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Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:30:37

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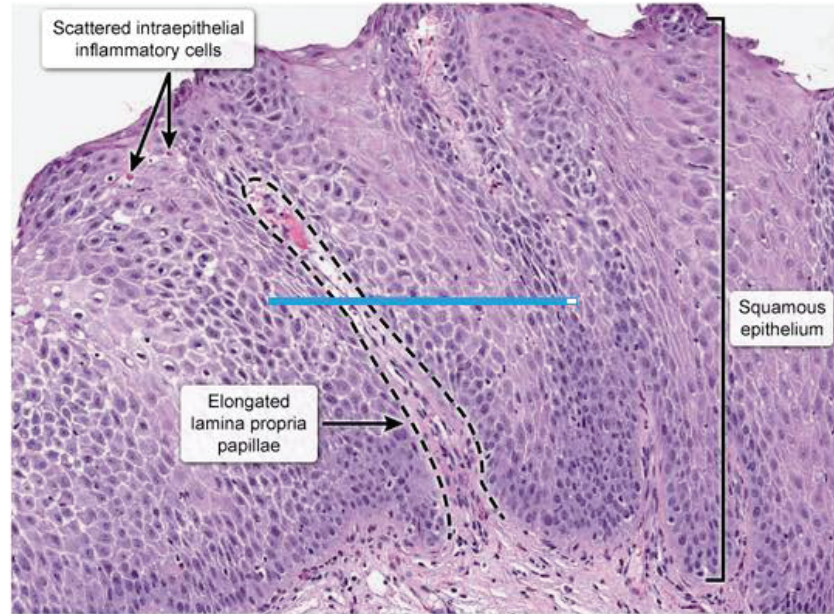
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End Block

(Choice A) Benign tumors of the esophagus (most commonly leiomyomas) are rare and slow-growing. On

Exhibit Display

Reflux esophagitis





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

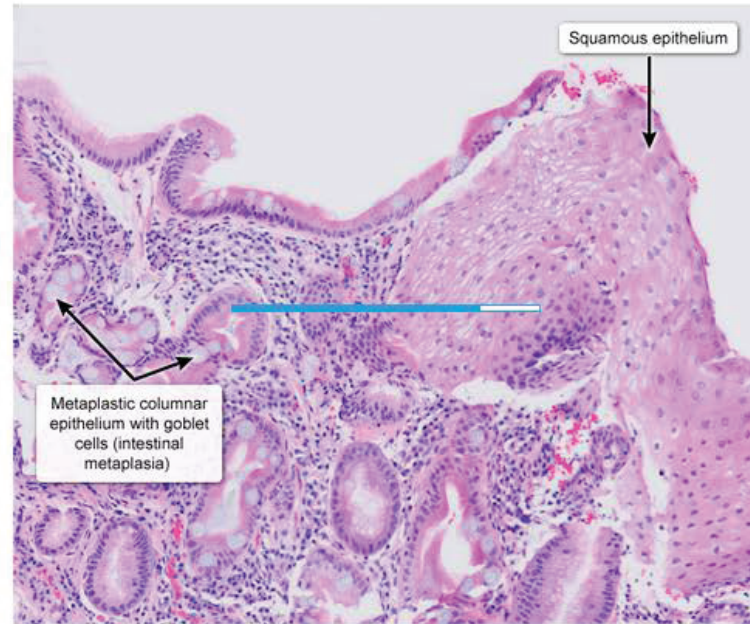
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Settings

(Choice A) Benign tumors of the esophagus (most commonly leiomyomas) are rare and slow-growing. On

## Exhibit Display

## Barrett esophagus



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:30:37

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 42-year-old man comes to the office due to progressive fatigue, nausea, and itchiness. On review of systems, the patient admits that he occasionally has bloody stools. Medical history is unremarkable. Examination shows scleral icterus. Liver biopsy reveals fibrous obliteration of intrahepatic small bile ducts with concentric replacement by connective tissue. Which of the following is the most likely diagnosis?

- ☐ A. Autoimmune hepatitis
- ☐ B. Cytomegalovirus infection
- ☐ C. Hemochromatosis
- ☐ D. Primary biliary cholangitis
- ☐ E. Primary sclerosing cholangitis

**Submit**

1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom




Settings

A 42-year-old man comes to the office due to progressive fatigue, nausea, and itchiness. On review of systems, the patient admits that he occasionally has bloody stools. Medical history is unremarkable. Examination shows scleral icterus. Liver biopsy reveals fibrous obliteration of intrahepatic small bile ducts with concentric replacement by connective tissue. Which of the following is the most likely diagnosis?

- ☐ A. Autoimmune hepatitis (2%)
- ☐ B. Cytomegalovirus infection (0%)
- ☐ C. Hemochromatosis (0%)
- ☐ D. Primary biliary cholangitis (18%)
- ☒ E. Primary sclerosing cholangitis (77%)

Correct

 77%  
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Explanation

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

## Autoimmune liver disease

	Autoimmune hepatitis	Primary biliary cholangitis	Primary sclerosing cholangitis
<b>Epidemiology</b>	• Female > male	• Female >> male	• Male > female
<b>Associations</b>	• Other autoimmune disorders	• Other autoimmune disorders	• IBD (particularly UC)
<b>Liver injury pattern</b>	• Hepatocellular (↑ transaminases)	• Cholestatic (↑ alkaline phosphatase)	• Cholestatic (↑ alkaline phosphatase)
<b>Antibodies</b>	• Anti-smooth muscle • Antinuclear*	• Antimitochondrial • Antinuclear*	• ± p-ANCA*
<b>Histology</b>	• Interface hepatitis (portal & periportal lymphoplasmocytic	• Florid duct lesion (granulomatous destruction of small bile	• Fibrous obliteration of bile ducts with concentric periductal deposition of connective tissue (onion-skin



1



Feedback



Suspend



End Block





Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

<b>Liver injury pattern</b>	<ul style="list-style-type: none"> <li>• Hepatocellular (↑ transaminases)</li> </ul>	<ul style="list-style-type: none"> <li>• Cholestatic (↑ alkaline phosphatase)</li> </ul>	<ul style="list-style-type: none"> <li>• Cholestatic (↑ alkaline phosphatase)</li> </ul>
<b>Antibodies</b>	<ul style="list-style-type: none"> <li>• Anti-smooth muscle</li> <li>• Antinuclear*</li> </ul>	<ul style="list-style-type: none"> <li>• Antimitochondrial</li> <li>• Antinuclear*</li> </ul>	<ul style="list-style-type: none"> <li>• ± p-ANCA*</li> </ul>
<b>Histology</b>	<ul style="list-style-type: none"> <li>• Interface hepatitis (portal &amp; periportal lymphoplasmocytic infiltrate)</li> </ul>	<ul style="list-style-type: none"> <li>• Florid duct lesion (granulomatous destruction of small bile ducts)</li> </ul>	<ul style="list-style-type: none"> <li>• Fibrous obliteration of bile ducts with concentric periductal deposition of connective tissue (onion-skin pattern)</li> </ul>

\*Nonspecific.

**IBD** = inflammatory bowel disease; **p-ANCA** = perinuclear antineutrophil cytoplasmic antibodies; **UC** = ulcerative colitis.

This patient with fatigue, nausea, pruritus, and scleral icterus has characteristic biopsy findings associated with **primary sclerosing cholangitis** (PSC), a chronic disorder characterized by inflammation, fibrosis, and stricture of the intrahepatic and extrahepatic bile ducts. Histologic features include **fibrous**



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

ulcerative colitis.

This patient with fatigue, nausea, pruritus, and scleral icterus has characteristic biopsy findings associated with **primary sclerosing cholangitis** (PSC), a chronic disorder characterized by inflammation, fibrosis, and stricture of the intrahepatic and extrahepatic bile ducts. Histologic features include **fibrous obliteration of the bile ducts** and **concentric periductal deposition of connective tissue**, which resembles an onion skin–like pattern. PSC affects men disproportionately and has a strong association with **ulcerative colitis**, likely explaining this patient's bloody stools.

Manifestations of PSC are related to cholestasis and include **pruritus**, jaundice, and fatigue. Laboratory findings also reflect a **cholestatic pattern of liver injury** and include elevated alkaline phosphatase levels, direct hyperbilirubinemia, and normal to mildly elevated aminotransferases. Common nonspecific findings include hypergammaglobulinemia and elevated P-ANCA. The diagnosis is confirmed with cholangiography (eg, MR cholangiopancreatography, endoscopic retrograde cholangiopancreatography) demonstrating multifocal bile duct stricture with segmental dilations.

**(Choice A)** Autoimmune hepatitis can cause fatigue, pruritus, and jaundice but is characterized histologically by portal and periportal lymphoplasmacytic infiltration. It is usually diagnosed in women with other autoimmune conditions (eg, celiac disease).







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** Autoimmune hepatitis can cause fatigue, pruritus, and jaundice but is characterized histologically by portal and periportal lymphoplasmacytic infiltration. It is usually diagnosed in women with other autoimmune conditions (eg, celiac disease).

**(Choice B)** Cytomegalovirus infection can cause hepatitis; however, microscopy typically reveals large cells with basophilic intracytoplasmic and intranuclear inclusions (eg, owl's eye appearance). In addition, it typically occurs in immunocompromised individuals (eg, transplant patients).

**(Choice C)** Hemochromatosis leads to excessive hepatic iron storage, which results in visible **iron deposits** within hepatocytes. It is typically associated with diabetes, skin hyperpigmentation, arthralgias, and cardiomyopathy.

**(Choice D)** Primary biliary cholangitis also causes cholestasis with jaundice and pruritus; however, it is characterized histologically by inflammation and granulomatous destruction of the small bile ducts (eg, florid duct lesions). In addition, it is much more common in women, and is not usually associated with inflammatory bowel disease.

**Educational objective:**

Primary sclerosing cholangitis is characterized by inflammation, fibrosis, and stricture of intrahepatic and extrahepatic bile ducts. Histologic findings include fibrous obliteration of bile ducts and periductal



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

cells with basophilic intracytoplasmic and intranuclear inclusions (eg, owl's eye appearance). In addition, it typically occurs in immunocompromised individuals (eg, transplant patients).

**(Choice C)** Hemochromatosis leads to excessive hepatic iron storage, which results in visible **iron deposits** within hepatocytes. It is typically associated with diabetes, skin hyperpigmentation, arthralgias, and cardiomyopathy.

**(Choice D)** Primary biliary cholangitis also causes cholestasis with jaundice and pruritus; however, it is characterized histologically by inflammation and granulomatous destruction of the small bile ducts (eg, florid duct lesions). In addition, it is much more common in women, and is not usually associated with inflammatory bowel disease.

### Educational objective:

Primary sclerosing cholangitis is characterized by inflammation, fibrosis, and stricture of intrahepatic and extrahepatic bile ducts. Histologic findings include fibrous obliteration of bile ducts and periductal concentric connective tissue deposition (eg, onion-skin pattern). Manifestations reflect cholestasis and include jaundice, pruritus, fatigue, and a cholestatic pattern of liver injury (ie, elevated alkaline phosphatase, direct hyperbilirubinemia).



1



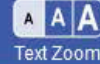
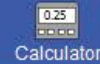
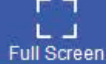
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A 52-year-old postmenopausal woman comes to the office for evaluation of several months of episodic abdominal discomfort and nausea, especially after a fatty meal. She has no past medical history and does not use tobacco, alcohol, or illicit drugs. Her BMI is 33 kg/m<sup>2</sup>. Physical examination shows a soft, nontender abdomen with normal bowel sounds. Liver span is 8 cm. Murphy sign is negative. Abdominal x-ray reveals no calcifications, but abdominal ultrasound shows a small, non-obstructing gallstone. The patient prefers nonoperative management. Which of the following would best treat this patient's condition?

- ☐ A. Bile acid supplement
- ☐ B. Cholestyramine therapy
- ☐ C. Estrogen replacement therapy
- ☐ D. Fenofibrate therapy
- ☐ E. Iron chelation therapy
- ☐ F. Phosphate-binding agent
- ☐ G. Rapid weight loss





abdominal discomfort and nausea, especially after a fatty meal. She has no past medical history and does not use tobacco, alcohol, or illicit drugs. Her BMI is 33 kg/m<sup>2</sup>. Physical examination shows a soft, nontender abdomen with normal bowel sounds. Liver span is 8 cm. Murphy sign is negative. Abdominal x-ray reveals no calcifications, but abdominal ultrasound shows a small, non-obstructing gallstone. The patient prefers nonoperative management. Which of the following would best treat this patient's condition?

- ☒ A. Bile acid supplement (46%)
- ☐ B. Cholestyramine therapy (31%)
- ☐ C. Estrogen replacement therapy (2%)
- ☐ D. Fenofibrate therapy (8%)
- ☐ E. Iron chelation therapy (0%)
- ☐ F. Phosphate-binding agent (4%)
- ☐ G. Rapid weight loss (5%)

Correct

46%

39 secs

02/11/2021

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Previous



Next



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Lab Values



Notes



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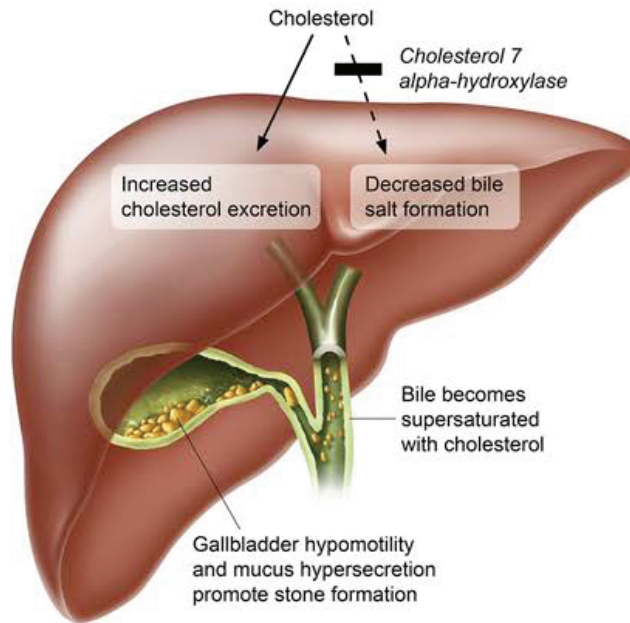
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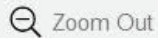
## Formation of cholesterol gallstones



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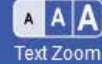
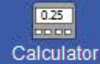
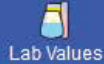
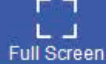
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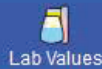


**Cholesterol gallstones** are the most common type of gallstone. They are primarily composed of cholesterol monohydrate crystals but can contain variable amounts of calcium salts, bilirubin, and mucin. Normally, bile acids and phospholipids solubilize the cholesterol to prevent stone formation. Decreased amounts of bile acids and phospholipids can cause the bile to become supersaturated with cholesterol, allowing it to crystallize and form cholesterol gallstones. Risk factors for stone formation include increasing age, obesity, excessive bile salt loss (eg, terminal ileum disease), and female sex.

Cholecystectomy is the preferred treatment for symptomatic gallstones. However, medical therapy is an option in patients refusing surgery or with high surgical risk. Administration of **hydrophilic bile acids** (eg, ursodeoxycholic acid) reduces cholesterol secretion and increases biliary bile acid concentration. This improves cholesterol solubility and **promotes gallstone dissolution**. Although the response to medical therapy is good in patients with mild symptoms and small stones, there is a high rate of gallstone recurrence.

**(Choice B)** Bile acid sequestrants (eg, cholestyramine) decrease enterohepatic recirculation of bile acids (increase gallstone risk). However, they also stimulate the conversion of cholesterol to bile acids and increase biliary motility (decrease gallstone risk). The net result is no significant change in the risk of gallstones.





gallstones.

**(Choice C)** Estrogen increases cholesterol secretion and progesterone reduces bile acid secretion, ultimately causing bile to become supersaturated with cholesterol. Progesterone also slows gallbladder emptying, which causes bile stasis and further promotes gallstone formation.

**(Choice D)** Fibrates increase cholesterol content in bile, which increases the risk of gallstones.

**(Choice E)** Iron chelation therapy is used to treat iron overload syndromes but has no significant effect on gallstones.

**(Choice F)** Phosphate-binding agents can lower serum phosphate in chronic kidney disease and dialysis patients but do not significantly affect gallstones.

**(Choice G)** Very low-calorie diets with decreased caloric intake and rapid weight loss can lead to bile stasis and increased cholesterol mobilization, increasing the risk of gallstone formation.

**Educational objective:**

Medical therapy to dissolve cholesterol gallstones is an option in patients refusing cholecystectomy or with high surgical risk. Hydrophilic bile acids (eg, ursodeoxycholic acid) improve cholesterol solubility by reducing the amount of cholesterol secreted into the bile and increasing biliary bile acid concentration.







A 76-year-old woman with type 2 diabetes mellitus is brought to the hospital after her family found her unresponsive in the morning. Her daughter reports that they were busy the previous day with many activities that required extensive walking. The patient ate less dinner than usual because she felt tired. She has discontinued several antidiabetic medications in the past due to medication intolerance but recently has had good glycemic control with a single medication. Blood pressure is 140/80 mm Hg and pulse is 102/min. The patient is diaphoretic and responds only to pain. Pupils are equal, round, and reactive to light. Cardiopulmonary examination is normal. Blood glucose is 34 mg/dL. The patient's condition rapidly improves after administration of an intravenous bolus of dextrose, but she becomes confused again several hours later. Repeat blood glucose is 39 mg/dL. Which of the following medications is the most likely cause of this patient's current condition?

- ☐ A. Acarbose
- ☐ B. Glyburide
- ☐ C. Metformin
- ☒ D. Pioglitazone
- ☐ E. Repaglinide

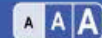




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- ☐ B. Glyburide
- ☐ C. Metformin
- ☐ D. Pioglitazone
- ☐ E. Repaglinide
- ☐ F. Sitagliptin

**Submit**



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- ☐ A. Acarbose (4%)
- ☒ B. Glyburide (55%)
- ☐ C. Metformin (11%)
- ☐ D. Pioglitazone (9%)
- ☐ E. Repaglinide (12%)
- ☐ F. Sitagliptin (6%)

Correct



55%

Answered correctly



02 mins, 06 secs

Time Spent



10/09/2020

Last Updated

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### Noninsulin antidiabetic agents for type 2 diabetes mellitus

Agent	Mechanism of action	Side effects
<b>Insulin secretagogues</b> <ul style="list-style-type: none"><li>• Sulfonylureas</li><li>• Meglitinides</li></ul>	↑ Insulin secretion by inhibiting $\beta$ -cell $K_{ATP}$ channels	<ul style="list-style-type: none"><li>• Hypoglycemia</li><li>• Weight gain</li></ul>
<b>Biguanides</b> <ul style="list-style-type: none"><li>• Metformin</li></ul>	Stimulate AMPK & inhibit mitochondrial gluconeogenesis, ↓ hepatic glucose production & ↑ peripheral glucose uptake	<ul style="list-style-type: none"><li>• Diarrhea</li><li>• Lactic acidosis</li></ul>
<b>Thiazolidinediones</b> <ul style="list-style-type: none"><li>• Pioglitazone</li></ul>	Activate transcription regulator PPAR- $\gamma$ , ↓ insulin resistance	<ul style="list-style-type: none"><li>• Fluid retention/heart failure</li><li>• Weight gain</li></ul>
<b>GLP-1 agonists</b> <ul style="list-style-type: none"><li>• Exenatide</li><li>• Liraglutide</li></ul>	↑ Glucose-dependent insulin secretion, ↓ glucagon secretion, delayed gastric emptying	<ul style="list-style-type: none"><li>• Pancreatitis</li><li>• Weight loss</li></ul>





- Exenatide
- Liraglutide

↑ Glucose-dependent insulin secretion, ↓ glucagon secretion, delayed gastric emptying

- Pancreatitis
- Weight loss

### DPP4 inhibitors

- Sitagliptin
- Saxagliptin

↑ Endogenous GLP-1 & GIP levels

- Nasopharyngitis

### α-glucosidase inhibitors

- Acarbose
- Miglitol

↓ Intestinal disaccharide absorption

- Diarrhea
- Flatulence

### SGLT2 inhibitors

- Canagliflozin
- Dapagliflozin

↑ Renal glucose excretion

- Urinary tract infections
- Hypotension

**AMPK** = adenosine monophosphate-activated protein kinase; **DPP4** = dipeptidyl peptidase-4; **GIP** = gastric inhibitory polypeptide; **GLP-1** = glucagonlike peptide-1; **K<sub>ATP</sub>** = ATP-sensitive potassium; **PPAR-γ** = peroxisome proliferator-activated receptor γ; **SGLT2** = sodium-glucose cotransporter 2.





This patient's **persistent hypoglycemia** is most likely due to an **excessive insulin response** from her diabetes medication. Given the available answer options, she was most likely taking a **sulfonylurea** (eg, glyburide).

Sulfonylurea bind to a receptor on pancreatic beta cells and inhibit the ATP-sensitive potassium channel. This alters the cell's resting potential and allows calcium influx, leading to exocytosis of insulin. The net result is increased insulin secretion **independent of blood glucose** concentrations, which confers a significant risk of hypoglycemia.

Hypoglycemia with sulfonylureas can be induced by exercise, missed meals, acute illness, or initiation of additional antidiabetic medications. The risk is greater in the elderly and in patients with metabolic dysfunction (eg, chronic kidney disease, hepatic impairment). As in this patient, sulfonylurea-induced hypoglycemia may reoccur, even after successful initial treatment, until the drug has been cleared from the circulation.

**(Choice A)** Acarbose is an alpha-glucosidase inhibitor that decreases intestinal glucose absorption and blunts the postprandial rise in serum glucose. Although it can increase insulin sensitivity in the elderly, acarbose is not associated with significant hypoglycemia.







**(Choice C)** Metformin is a biguanide that decreases hepatic glucose production and intestinal glucose absorption and increases peripheral glucose uptake and utilization. Metformin has rarely been associated with lactic acidosis but does not typically cause hypoglycemia.

**(Choice D)** Thiazolidinediones (eg, pioglitazone) increase insulin sensitivity by increasing glucose utilization and decreasing glucose production in adipose tissue, muscle, and liver. Thiazolidinediones have been associated with cardiac side effects (eg, heart failure) but carry a low risk of hypoglycemia.

**(Choice E)** Meglitinides (eg, repaglinide) are insulin secretagogues that induce pancreatic insulin secretion even when blood glucose levels are normal. Although they can cause hypoglycemia, they have a very short half-life (~1 hr) and are less likely than sulfonylureas to cause *prolonged* hypoglycemia, as in this patient.

**(Choice F)** Sitagliptin is a dipeptidyl peptidase 4 inhibitor that increases *glucose-dependent* insulin release from the pancreatic beta cells. Its effect on insulin release diminishes as glucose levels approach normal, and so it does not usually cause hypoglycemia.

### Educational objective:

Sulfonylureas (eg, glyburide, glimepiride) increase insulin secretion by pancreatic beta cells independent of blood glucose concentration. These medications have a high incidence of hypoglycemia, especially in the





(Choice D) Thiazolidinediones (eg, pioglitazone) increase insulin sensitivity by increasing glucose

utilization and decreasing glucose production in adipose tissue, muscle, and liver. Thiazolidinediones have been associated with cardiac side effects (eg, heart failure) but carry a low risk of hypoglycemia.

(Choice E) Meglitinides (eg, repaglinide) are insulin secretagogues that induce pancreatic insulin secretion even when blood glucose levels are normal. Although they can cause hypoglycemia, they have a very short half-life (~1 hr) and are less likely than sulfonylureas to cause *prolonged* hypoglycemia, as in this patient.

(Choice F) Sitagliptin is a dipeptidyl peptidase 4 inhibitor that increases *glucose-dependent* insulin release from the pancreatic beta cells. Its effect on insulin release diminishes as glucose levels approach normal, and so it does not usually cause hypoglycemia.

### Educational objective:

Sulfonylureas (eg, glyburide, glimepiride) increase insulin secretion by pancreatic beta cells independent of blood glucose concentration. These medications have a high incidence of hypoglycemia, especially in the elderly.

### References

- [Minimizing hypoglycemia in diabetes.](#)



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A 58-year-old man is evaluated for a thyroid nodule. The patient first noticed a painless neck lump 2 months ago, which has progressively enlarged. He has had no heat or cold intolerance, recent weight changes, or difficulty breathing or swallowing. Medical history is notable for well-controlled hypertension. The patient has no history of radiation exposure or family history of thyroid diseases. Physical examination shows a firm, nontender nodule in the right thyroid lobe. Serum TSH level is normal, and ultrasonography shows a 4-cm solid nodule in the right thyroid lobe. Fine-needle aspiration biopsy shows a large number of follicular cells dispersed in clusters and microfollicles. The patient undergoes right thyroid lobectomy. Which of the following histologic findings would confirm a diagnosis of follicular thyroid carcinoma in this patient?

- ☐ A. C-cell hyperplasia
- ☐ B. Cells with empty appearing nuclei
- ☐ C. Hürthle cells
- ☐ D. Lymphocytic germinal centers
- ☐ E. Multinucleated giant cells







months ago, which has progressively enlarged. He has had no heat or cold intolerance, recent weight changes, or difficulty breathing or swallowing. Medical history is notable for well-controlled hypertension. The patient has no history of radiation exposure or family history of thyroid diseases. Physical examination shows a firm, nontender nodule in the right thyroid lobe. Serum TSH level is normal, and ultrasonography shows a 4-cm solid nodule in the right thyroid lobe. Fine-needle aspiration biopsy shows a large number of follicular cells dispersed in clusters and microfollicles. The patient undergoes right thyroid lobectomy. Which of the following histologic findings would confirm a diagnosis of follicular thyroid carcinoma in this patient?

- ☐ A. C-cell hyperplasia
- ☐ B. Cells with empty appearing nuclei
- ☐ C. Hürthle cells
- ☐ D. Lymphocytic germinal centers
- ☐ E. Multinucleated giant cells
- ☐ F. Tumor capsular invasion





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

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The patient has no history of radiation exposure or family history of thyroid diseases. Physical examination shows a firm, nontender nodule in the right thyroid lobe. Serum TSH level is normal, and ultrasonography shows a 4-cm solid nodule in the right thyroid lobe. Fine-needle aspiration biopsy shows a large number of follicular cells dispersed in clusters and microfollicles. The patient undergoes right thyroid lobectomy. Which of the following histologic findings would confirm a diagnosis of follicular thyroid carcinoma in this patient?

- ☐ A. C-cell hyperplasia (5%)
- ☐ B. Cells with empty appearing nuclei (10%)
- ☐ C. Hürthle cells (9%)
- ☐ D. Lymphocytic germinal centers (8%)
- ☐ E. Multinucleated giant cells (3%)
- ☒ F. Tumor capsular invasion (63%)

Correct

63%

35 secs

08/22/2020

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Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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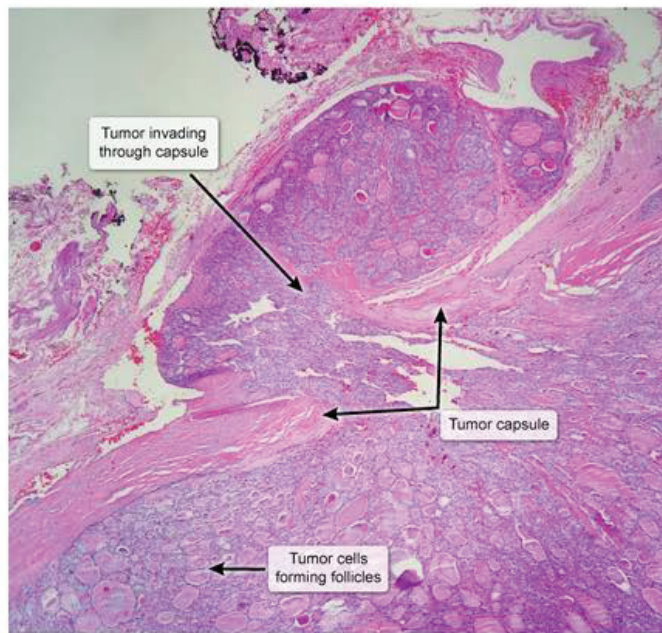
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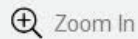
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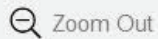
## Follicular thyroid carcinoma



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This euthyroid patient has a slowly enlarging, firm, painless thyroid nodule and fine-needle aspiration (FNA) results indicative of a **follicular neoplasm** (eg, numerous follicular cells and microfollicles). Most follicular thyroid neoplasms are benign follicular adenomas, but 15%-30% can be malignant follicular carcinomas. Both types of follicular neoplasms have a similar appearance on ultrasound and FNA.

Differentiating between benign and malignant follicular lesions can only be accomplished by histologic examination of the entire tumor (eg, thyroidectomy).

- Follicular adenomas (the most common benign thyroid neoplasm) display numerous neoplastic follicular cells and microfollicles on histology but are completely **encapsulated**.
- In contrast, **follicular thyroid carcinomas (FTCs)** are characterized by **invasion of the tumor capsule** and/or surrounding blood vessels.

This propensity of FTCs to invade surrounding blood vessels accounts for their tendency to metastasize via **hematogenous spread** to distant tissues (eg, bone, lung).

**(Choice A)** Medullary thyroid carcinomas (MTCs) can develop sporadically or in patients with an inherited *RET* proto-oncogene mutation (eg, multiple endocrine neoplasia 2a or 2b). In patients with this germline





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

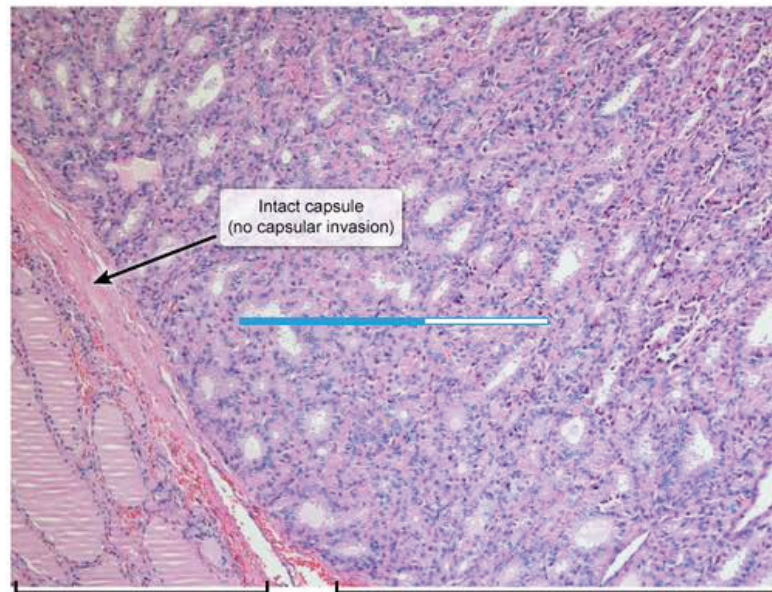
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## Follicular adenoma



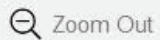
Normal thyroid

Neoplastic cells forming follicles

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**(Choice A)** Medullary thyroid carcinomas (MTCs) can develop sporadically or in patients with an inherited *RET* proto-oncogene mutation (eg, multiple endocrine neoplasia 2a or 2b). In patients with this germline mutation, **C-cell hyperplasia** is often found as a precursor to a malignant lesion. Like normal C cells, malignant C cells secrete calcitonin, which can be used both for initial detection and monitoring postoperatively.

**(Choice B)** Papillary thyroid carcinoma (the most common type of thyroid malignancy) has distinct cytologic and histologic features. These include laminar calcifications (**psammoma bodies**), large cells with ground-glass cytoplasm, and cells with pale, empty-appearing nuclei (Orphan Annie–eye nuclei) with nuclear inclusion bodies and **nuclear grooves**. Unlike FTC, papillary thyroid carcinoma can be diagnosed on FNA results.

**(Choice C)** Hürthle cells are large, polygonal cells with granular, eosinophilic cytoplasm due to large quantities of mitochondria. They are seen in a wide variety of neoplastic and nonneoplastic thyroid lesions (eg, FTCs and follicular adenomas). Therefore, they would not be of benefit in differentiating between benign and malignant follicular lesions.

**(Choice D)** Chronic autoimmune (Hashimoto) thyroiditis typically presents with signs of primary hypothyroidism (eg, weight gain, cold intolerance, elevated TSH) due to autoimmune destruction of the







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Previous



Next



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Tutorial



Lab Values



Notes



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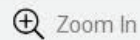
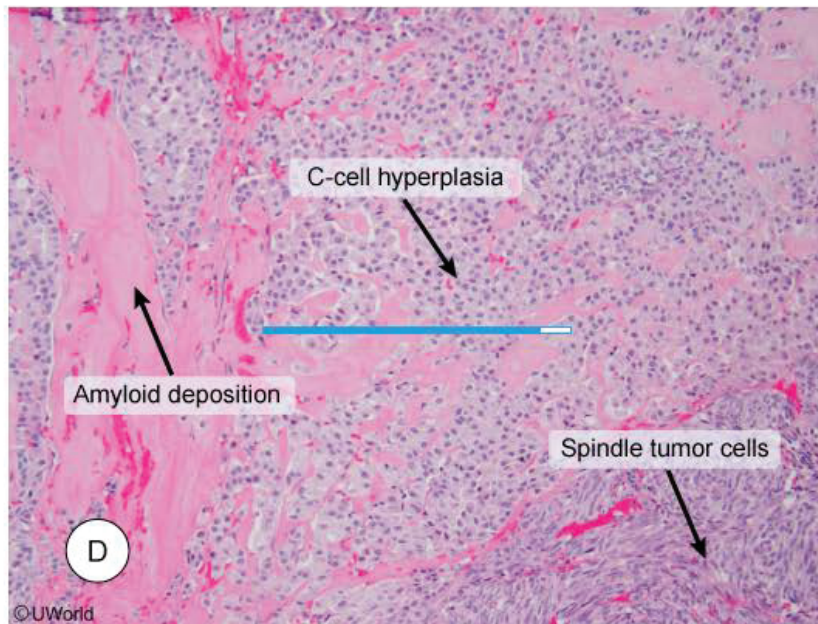


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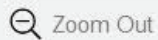


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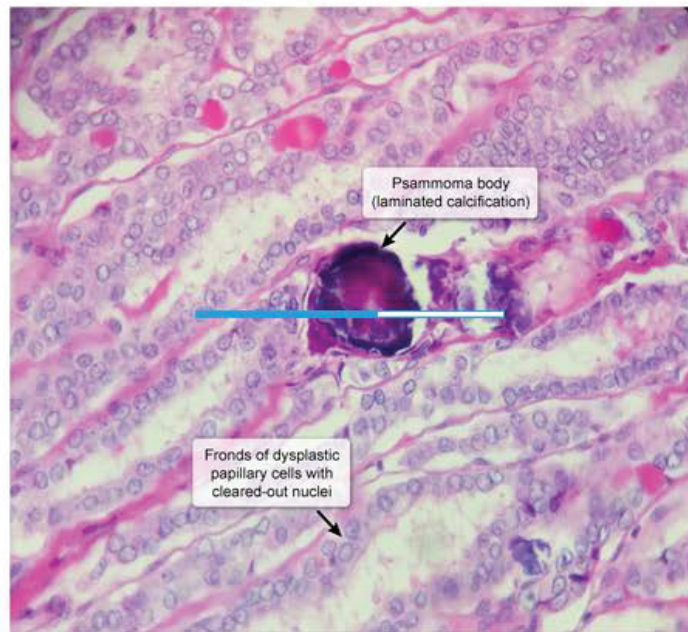


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## Papillary thyroid carcinoma



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Item 2 of 9

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Previous

Next

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Tutorial

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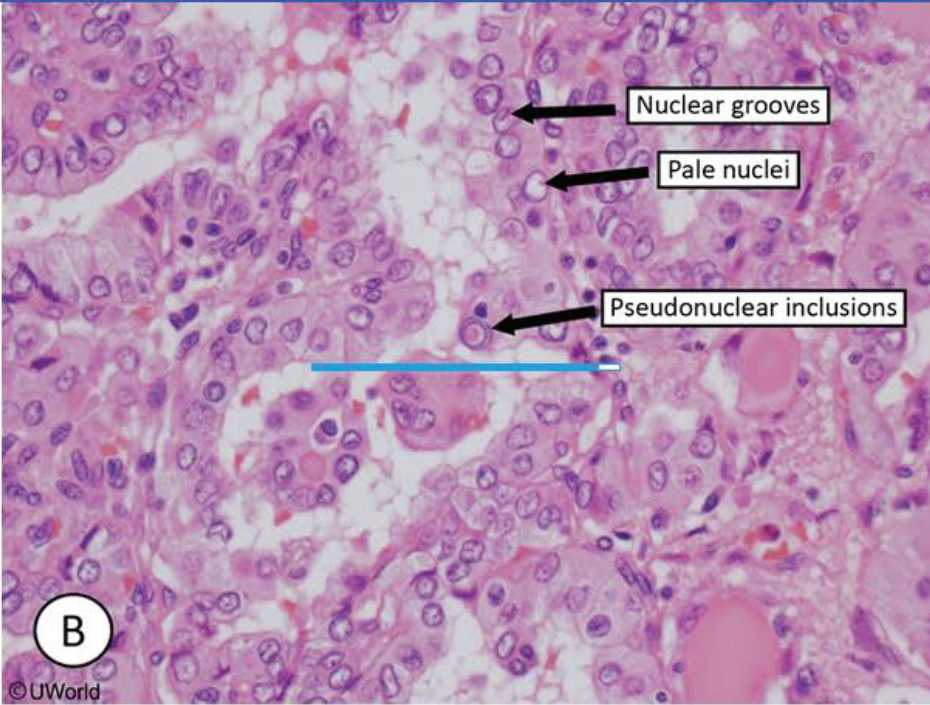
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Nuclear grooves

Pale nuclei

Pseudonuclear inclusions

B

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hypothyroidism (eg, weight gain, cold intolerance, elevated TSH) due to autoimmune destruction of the





quantities of mitochondria. They are seen in a wide variety of neoplastic and nonneoplastic thyroid lesions (eg, FTCs and follicular adenomas). Therefore, they would not be of benefit in differentiating between benign and malignant follicular lesions.

**(Choice D)** Chronic autoimmune (Hashimoto) thyroiditis typically presents with signs of primary hypothyroidism (eg, weight gain, cold intolerance, elevated TSH) due to autoimmune destruction of the thyroid gland. Histology shows inflammation and **lymphocytic germinal centers** in the thyroid gland.

**(Choice E)** Multinucleated giant cells are seen in many thyroid conditions, including thyroiditis, cystic degeneration, and papillary thyroid carcinoma. They are not typically seen in follicular lesions.

### Educational objective:

Follicular neoplasms typically present as slowly enlarging, painless thyroid nodules. Differentiation between a follicular adenoma and follicular thyroid carcinoma is not possible using only fine-needle aspiration results. Histologic evidence of invasion of the tumor capsule and/or surrounding blood vessels is needed to diagnose follicular thyroid carcinoma.

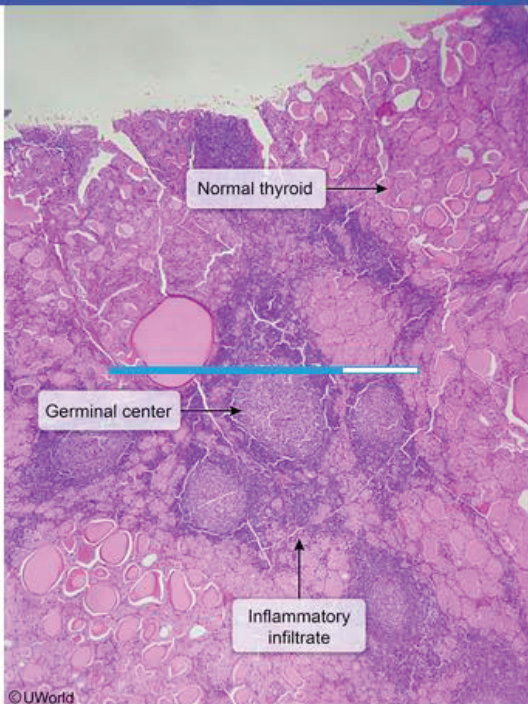
### References

- [How to interpret thyroid fine-needle aspiration biopsy reports: a guide for the busy radiologist in the era of the Bethesda Classification System.](#)



quantities of mitochondria. They are seen in a wide variety of neoplastic and nonneoplastic thyroid lesions

Exhibit Display



Zoom In Zoom Out Reset New Existing My Notebook



A 34-year-old man comes to the clinic due to frequent clumsiness. For the last 6 months, he has had repeated minor injuries from walking into doorways and stationary objects. The patient was also reprimanded at work for causing his supervisor to spill coffee when he bumped into her in the hallway. Medical history is notable for recurrent renal stones; following a subsequent diagnostic evaluation, the patient underwent definitive treatment with neck surgery 3 years ago. Family history is unavailable as the patient was adopted. Physical examination reveals bitemporal visual field defects. Cranial nerves, motor strength, and deep-tendon reflexes are otherwise normal. In addition to brain imaging, this patient should also be screened for which of the following tumors?

- ☐ A. Adrenal
- ☐ B. Bone
- ☐ C. Breast
- ☐ D. Colonic
- ☐ E. Pancreatic







repeated minor injuries from walking into doorways and stationary objects. The patient was also reprimanded at work for causing his supervisor to spill coffee when he bumped into her in the hallway. Medical history is notable for recurrent renal stones; following a subsequent diagnostic evaluation, the patient underwent definitive treatment with neck surgery 3 years ago. Family history is unavailable as the patient was adopted. Physical examination reveals bitemporal visual field defects. Cranial nerves, motor strength, and deep-tendon reflexes are otherwise normal. In addition to brain imaging, this patient should also be screened for which of the following tumors?

- ☐ A. Adrenal (24%)
- ☐ B. Bone (9%)
- ☐ C. Breast (2%)
- ☐ D. Colonic (2%)
- ☒ E. Pancreatic (60%)

Correct

60%  
Answered correctly01 min  
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Last Updated

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Feedback



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### Classification of multiple endocrine neoplasia

#### Type 1

- **Primary hyperparathyroidism** (parathyroid adenomas or hyperplasia)
- Pituitary tumors (prolactin, visual defects)
- Pancreatic tumors (especially gastrinomas)

#### Type 2A

- **Medullary thyroid cancer** (calcitonin)
- Pheochromocytoma
- Primary hyperparathyroidism (parathyroid hyperplasia)

#### Type 2B

- **Medullary thyroid cancer** (calcitonin)
- Pheochromocytoma
- Mucosal neuromas/marfanoid habitus

**Multiple endocrine neoplasia type 1 (MEN1)** is caused by mutations in the *MEN1* tumor suppressor gene and is characterized by tumors of the **par**athyroid gland, **pit**uitary, and **pan**creas (the "**3 Ps**"). Primary hyperparathyroidism is often the initial manifestation and usually presents with asymptomatic





**Multiple endocrine neoplasia type 1 (MEN1)** is caused by mutations in the *MEN1* tumor suppressor gene and is characterized by tumors of the **parathyroid** gland, **pituitary**, and **pancreas** (the "**3 Ps**"). Primary hyperparathyroidism is often the initial manifestation and usually presents with asymptomatic hypercalcemia or **renal stones**. Prolactin-secreting adenomas (prolactinomas) are the most common pituitary tumors. In premenopausal women, prolactinomas typically present with metabolic symptoms (eg, menstrual irregularities, galactorrhea); in men and postmenopausal women they usually present later when tumor enlargement leads to mass effect symptoms such as headache or **bitemporal visual field defects** (causing clumsiness in this patient) due to compression of the optic chiasm.

**Entero-pancreatic neuroendocrine tumors** are the third major tumor type in MEN1. Gastrinoma (leading to Zollinger-Ellison syndrome) is the most common, followed by insulinoma and nonfunctional tumors. These tumors are often metastatic and are a frequent cause of tumor-related death in MEN1. This patient has visual field defects consistent with a pituitary mass lesion, which warrants cerebral imaging. In addition, he has a history of symptomatic hyperparathyroidism. Given these features of MEN1, he is also at increased risk for entero-pancreatic neuroendocrine tumors.

**(Choice A)** Pheochromocytoma is an adrenal medullary tumor that occurs commonly in MEN2A and 2B. However, this patient's visual field defect suggests a pituitary tumor, which is more characteristic of MEN1 (not associated with pheochromocytoma).







**(Choice A)** Pheochromocytoma is an adrenal medullary tumor that occurs commonly in MEN2A and 2B. However, this patient's visual field defect suggests a pituitary tumor, which is more characteristic of MEN1 (not associated with pheochromocytoma).

**(Choice B)** Primary bone tumors are not increased in MEN1, although malignant neuroendocrine tumors may occasionally metastasize to bone.

**(Choice C)** The major inherited syndromes associated with breast cancer include *BRCA1* and *BRCA2* mutations (breast, ovarian, uterine/fallopian tube, pancreatic cancers). Less common syndromes include Cowden syndrome, Li-Fraumeni syndrome, and Peutz-Jeghers syndrome. Hyperparathyroidism and pituitary tumors are not prominent manifestations of any of these syndromes and are more consistent with MEN1.

**(Choice D)** Familial adenomatous polyposis is associated with an increased risk of colon cancer and with adrenal adenomas and thyroid cancer.

### Educational objective:

Multiple endocrine neoplasia type 1 syndrome is characterized by tumors of the pituitary, parathyroid gland, and pancreas (the "3 Ps").

### References



1

2

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9

Item 4 of 9

Question Id: 226

Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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Text Zoom

Settings

A 60-year-old man is brought to the emergency department due to altered mental status. His wife says that he had a nagging cough that seemed to worsen over the past several months and that he began experiencing occasional dizziness earlier this week. Over the last couple of days, the patient has become increasingly confused, and today he "does not make any sense at all." He has no significant past medical history but has smoked a pack of cigarettes daily for the last 40 years. On physical examination, the patient is incoherent but has an otherwise normal neurologic examination.

Laboratory results are as follows:

Serum chemistry	
Sodium	120 mEq/L
Potassium	4.0 mEq/L
Blood urea nitrogen	12 mg/dL
Creatinine	0.8 mg/dL
Calcium	9.0 mg/dL

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www.ncbi.nlm.nih.gov/pubmed/26207052



patient is incoherent but has an otherwise normal neurologic examination.

Laboratory results are as follows:

Serum chemistry

Sodium 120 mEq/L

Potassium 4.0 mEq/L

Blood urea  
nitrogen 12 mg/dL

Creatinine 0.8 mg/dL

Calcium 9.0 mg/dL

Glucose 98 mg/dL

Plasma osmolality 250  
mOsm/kg

Urine drug screen negative







Plasma osmolality 250  
mOsm/kg

Urine drug screen negative

Chest x-ray reveals a mass in the right lung. Which of the following additional findings is most likely to be present in this patient?

- ☐ A. Bilateral crackles at the lung bases
- ☐ B. Elevated jugular venous pressure
- ☐ C. Maximally dilute urine
- ☐ D. Apparent euvolemia
- ☐ E. Peripheral edema

Submit





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Full Screen



Tutorial



Lab Values



Notes



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Settings

Plasma osmolality	250 mOsm/kg
Urine drug screen	negative

Chest x-ray reveals a **mass** in the right lung. Which of the following additional findings is most likely to be present in this patient?

- ☐ A. Bilateral crackles at the lung bases (5%)
- ☐ B. Elevated jugular venous pressure (11%)
- ☐ C. Maximally dilute urine (19%)
- ☒ D. Apparent euvoolemia (45%)
- ☐ E. Peripheral edema (18%)

Correct



45%

Answered correctly



01 min, 42 secs

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08/31/2020

Last Updated

Block Time Remaining: 00:05:23

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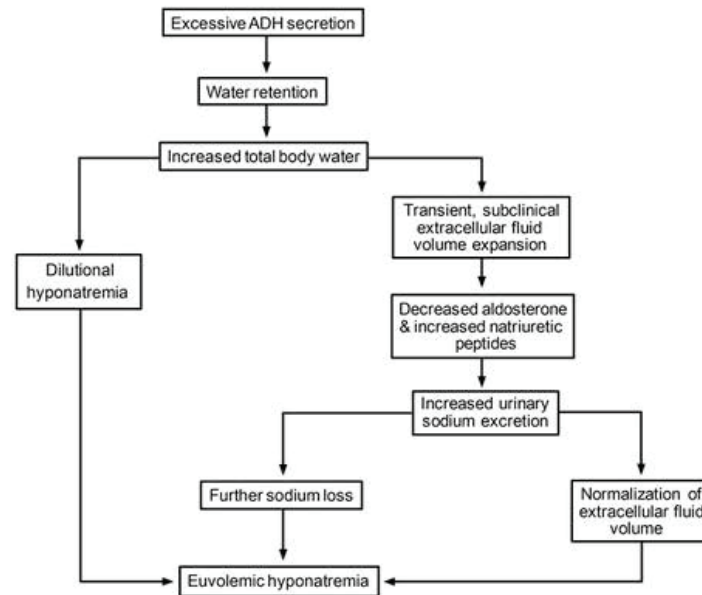


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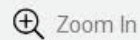
## Exhibit Display

## Pathophysiology of SIADH

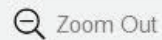


SIADH = syndrome of inappropriate antidiuretic hormone.

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The combination of hyponatremia and a lung mass is suggestive of the **syndrome of inappropriate antidiuretic hormone secretion (SIADH)**. ADH is normally produced in the hypothalamus and secreted from the posterior pituitary in response to changes in plasma osmolality and intravascular volume. However, **small cell lung carcinomas**, which are tumors of neuroendocrine origin, often release ADH independent of feedback inhibition (paraneoplastic effect). This inappropriate secretion of ADH leads to hyponatremia, decreased plasma osmolality, and elevated urine osmolality (which normally should be  $<100$  mOsm/kg given the degree of hyponatremia). The profound hyponatremia that occurs in SIADH can cause headache, weakness, **altered mental status**, and seizures.

In SIADH, increased ADH causes excessive water absorption by the kidneys, leading to a transient, subclinical hypervolemia. This mild increase in extracellular fluid volume suppresses the renin-aldosterone axis and stimulates the production of natriuretic peptides, leading to excretion of sodium in the urine (natriuresis). As a result, patients with SIADH have a clinically normal extracellular fluid volume and low plasma osmolality (**euvolemic hyponatremia**). Features of volume overload (eg, peripheral edema, pulmonary crackles, elevated jugular venous pressure) are not seen (**Choices A, B, and E**).

**(Choice C)** Patients with SIADH have inappropriately concentrated urine (generally  $>100$  mOsm/kg) for their degree of hyponatremia. Hyponatremia with a urine osmolality of  $<100$  mOsm/kg (maximally dilute urine) indicates appropriate suppression of ADH secretion (as would be seen in primary polydipsia).





## Exhibit Display

**Common causes of the syndrome of inappropriate antidiuretic hormone secretion**

- Central nervous system disruption (eg, stroke, infection, trauma & neurosurgery)
- Malignancies (eg, small cell lung carcinoma)
- Drugs (eg, desmopressin, chlorpropamide & carbamazepine)
- Pulmonary disorders (eg, pneumonia, tuberculosis & ventilator use)

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axis and stimulates the production of natriuretic peptides, leading to excretion of sodium in the urine (natriuresis). As a result, patients with SIADH have a clinically normal extracellular fluid volume and low plasma osmolality (**euvolemic hyponatremia**). Features of volume overload (eg, peripheral edema, pulmonary crackles, elevated jugular venous pressure) are not seen (**Choices A, B, and E**).

**(Choice C)** Patients with SIADH have inappropriately concentrated urine (generally  $>100$  mOsm/kg) for their degree of hyponatremia. Hyponatremia with a urine osmolality of  $<100$  mOsm/kg (maximally dilute urine) indicates appropriate suppression of ADH secretion (as would be seen in primary polydipsia).

### Educational objective:

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is characterized by low plasma sodium and osmolality, inappropriately concentrated urine, and clinically normal volume status (euvolemic hyponatremia). An important cause of SIADH is a paraneoplastic effect secondary to small cell carcinoma of the lung.

### References

- The syndrome of inappropriate antidiuresis: pathophysiology, clinical management and new therapeutic options.
- Management of hyponatremia: providing treatment and avoiding harm.







A 27-year-old man comes to the office due to recurrent episodes of muscle weakness. He has no other significant past medical history. The patient's weight has been stable for the past few years, and his current BMI is 23 kg/m<sup>2</sup>. His blood pressure is 190/110 mm Hg supine and 195/110 mm Hg standing. His heart rate is 70/min supine and 72/min standing. The rest of the physical examination is unremarkable. Laboratory evaluation shows very low plasma renin activity. Overactivity of which of the following structures is most likely responsible for this patient's symptoms?

- ☐ A. Chromaffin cells of the adrenals
- ☐ B. Extra-adrenal paraganglion cells
- ☐ C. Juxtaglomerular cells of the kidney
- ☐ D. Zona fasciculata of the adrenals
- ☐ E. Zona glomerulosa of the adrenals
- ☐ F. Zona reticularis of the adrenals

**Submit**

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Feedback



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A 27-year-old man comes to the office due to recurrent episodes of muscle weakness. He has no other significant past medical history. The patient's weight has been stable for the past few years, and his current BMI is 23 kg/m<sup>2</sup>. His blood pressure is 190/110 mm Hg supine and 195/110 mm Hg standing. His heart rate is 70/min supine and 72/min standing. The rest of the physical examination is unremarkable. Laboratory evaluation shows very low plasma renin activity. Overactivity of which of the following structures is most likely responsible for this patient's symptoms?

- ☐ A. Chromaffin cells of the adrenals (9%)
- ☐ B. Extra-adrenal paraganglion cells (0%)
- ☐ C. Juxtaglomerular cells of the kidney (4%)
- ☐ D. Zona fasciculata of the adrenals (5%)
- ☒ E. Zona glomerulosa of the adrenals (78%)
- ☐ F. Zona reticularis of the adrenals (0%)

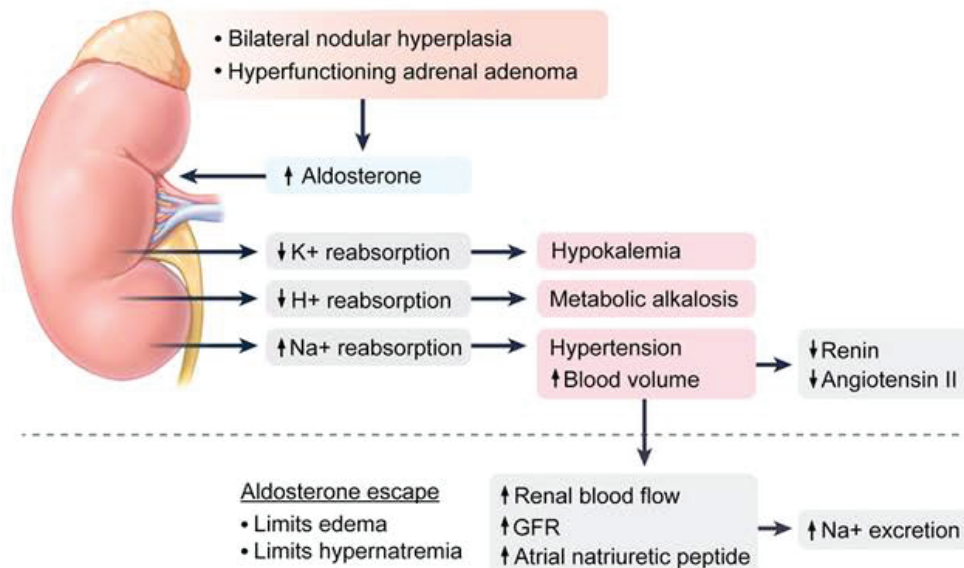




## Pathogenesis of primary hyperaldosteronism

### Exhibit Display

#### Pathogenesis of primary hyperaldosteronism (and aldosterone escape)



GFR = glomerular filtration rate.

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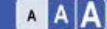
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GFR = glomerular filtration rate.

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This patient has features consistent with **primary hyperaldosteronism (PH)**, a very common cause of secondary hypertension. PH is usually due to increased secretion of mineralocorticoids from bilateral nodular hyperplasia of the adrenal zona glomerulosa or an aldosterone-producing adrenal adenoma (Conn syndrome).

The main effect of aldosterone is to stimulate absorption of sodium and excretion of potassium and hydrogen ions in the renal collecting tubules. Aldosterone secretion from the zona glomerulosa is normally regulated by angiotensin II and potassium levels. Overproduction of aldosterone can result in sodium retention, **hypertension**, and feedback suppression of the renin-angiotensin system (ie, **very low renin activity**). Some patients also develop metabolic alkalosis and **hypokalemia**, which can be exacerbated by increased distal tubule sodium delivery (eg, diuretics, increased sodium intake). Symptomatic hypokalemia may cause **muscle weakness**, cramps, and, occasionally, rhabdomyolysis and cardiac arrhythmias.

Despite the increase in sodium absorption, hyponatremia and pedal edema are rarely observed in PH due to the phenomenon of **aldosterone escape**. The high aldosterone levels lead to increased intravascular volume and therefore cause increased renal blood flow (with resulting pressure natriuresis) and augmented release of atrial natriuretic peptide. This ultimately results in increased sodium excretion by the renal tubules, which limits net sodium retention and prevents the development of overt volume overload and





tubules, which limits net sodium retention and prevents the development of overt volume overload and significant hypernatremia.

**(Choices A and B)** Pheochromocytomas are catecholamine-secreting tumors arising from the chromaffin cells of the adrenal medulla or extra-adrenal sympathetic chain, and typically present with severe hypertension. Pheochromocytomas stimulate the renin-angiotensin system due to high circulating catecholamine levels, and are associated with tachycardia and symptoms of catecholamine excess (eg, sweating, palpitations, headache).

**(Choice C)** Increased renin production by the juxtaglomerular apparatus leads to hypertension with elevated aldosterone levels. This typically occurs in the setting of renal artery stenosis with decreased renal blood flow. However, this patient's renin activity is suppressed.

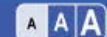
**(Choices D and F)** Hypersecretion from cells of the zona fasciculata or zona reticularis would lead to Cushing syndrome or hyperandrogenism, respectively. Cushing syndrome can cause hypertension and hypokalemia but is usually associated with weight gain and a Cushingoid body habitus (eg, central obesity, moon facies).

### Educational objective:

Primary hyperaldosteronism is caused by excessive aldosterone secretion, typically as a result of bilateral







hypertension. Pheochromocytomas stimulate the renin-angiotensin system due to high circulating catecholamine levels, and are associated with tachycardia and symptoms of catecholamine excess (eg, sweating, palpitations, headache).

**(Choice C)** Increased renin production by the juxtaglomerular apparatus leads to hypertension with elevated aldosterone levels. This typically occurs in the setting of renal artery stenosis with decreased renal blood flow. However, this patient's renin activity is suppressed.

**(Choices D and F)** Hypersecretion from cells of the zona fasciculata or zona reticularis would lead to Cushing syndrome or hyperandrogenism, respectively. Cushing syndrome can cause hypertension and hypokalemia but is usually associated with weight gain and a Cushingoid body habitus (eg, central obesity, moon facies).

### Educational objective:

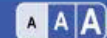
Primary hyperaldosteronism is caused by excessive aldosterone secretion, typically as a result of bilateral nodular hyperplasia of the zona glomerulosa or an aldosterone-producing adrenal adenoma. Clinical findings include hypertension, low plasma renin activity, hypokalemia, and metabolic alkalosis.

### References

- [Case detection, diagnosis, and treatment of patients with primary aldosteronism: an endocrine society](#)







A 56-year-old woman comes to the office due to progressive weight gain and fatigue over the last 4 months. She also has had increasing difficulty in lifting heavy objects and climbing stairs. The patient has moderate, persistent bronchial asthma for which she uses inhaled corticosteroids and beta-2 agonists. Family history is significant for colon cancer in her father. Blood pressure is 160/90 mm Hg and pulse is 80/min. On physical examination, there is symmetric proximal muscle weakness of the upper and lower extremities. Fasting plasma glucose level is 135 mg/dL and 24-hour urinary cortisol is increased. Further evaluation reveals that high-dose, but not low-dose, dexamethasone suppresses serum cortisol levels. Serum ACTH levels are high-normal. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Adrenal adenoma
- ☐ B. Adrenal carcinoma
- ☐ C. Exogenous glucocorticoids
- ☐ D. Pituitary adenoma
- ☐ E. Small cell lung cancer





moderate, persistent bronchial asthma for which she uses inhaled corticosteroids and beta-2 agonists. Family history is significant for colon cancer in her father. Blood pressure is 160/90 mm Hg and pulse is 80/min. On physical examination, there is symmetric proximal muscle weakness of the upper and lower extremities. Fasting plasma glucose level is 135 mg/dL and 24-hour urinary cortisol is increased. Further evaluation reveals that high-dose, but not low-dose, dexamethasone suppresses serum cortisol levels. Serum ACTH levels are high-normal. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Adrenal adenoma (9%)
- ☐ B. Adrenal carcinoma (1%)
- ☒ C. Exogenous glucocorticoids (9%)
- ☐ D. Pituitary adenoma (70%)
- ☐ E. Small cell lung cancer (9%)

Incorrect

Correct answer



70%



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11/25/2020

Last updated

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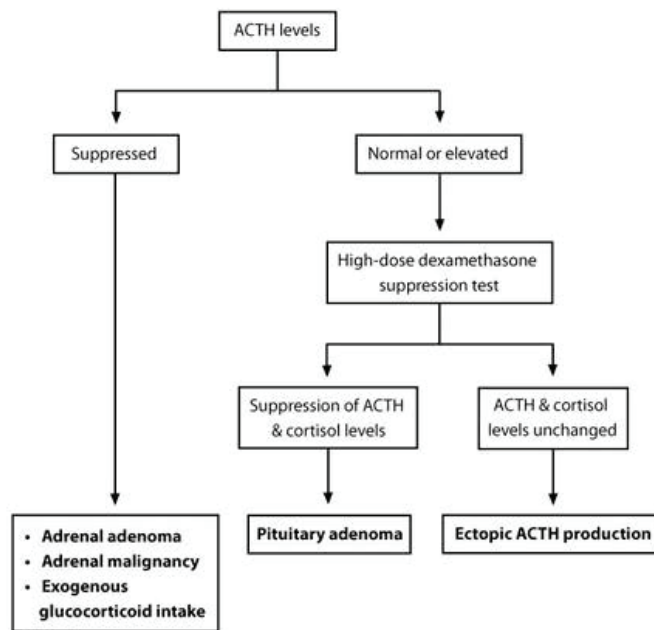


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## Exhibit Display

## Diagnosing the cause of Cushing syndrome



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This patient has weight gain, proximal muscle weakness, hypertension, and hyperglycemia, which are prominent features of **Cushing syndrome**. Screening tests for endogenous Cushing syndrome include **low-dose dexamethasone suppression testing**. In normal individuals, low doses of dexamethasone (a potent glucocorticoid) suppress ACTH and cortisol levels through negative feedback. However, in endogenous Cushing syndrome, ACTH and cortisol levels are not suppressed.

The most common causes of Cushing syndrome are shown in the flowchart and can be categorized on the basis of serum ACTH levels as either ACTH dependent (ACTH is high or inappropriately normal) or ACTH independent (ACTH is suppressed). In ACTH-dependent Cushing syndrome, if **high-dose dexamethasone suppresses ACTH** and cortisol secretion, a **pituitary source** of ACTH (ie, ACTH-secreting pituitary adenoma) is likely. In contrast, ectopic ACTH production (eg, from malignant tumors such as small cell lung cancer) is not suppressed by high-dose dexamethasone (**Choice E**).

This patient has excessive cortisol production that is suppressed by high-dose but not low-dose dexamethasone. This is consistent with an ACTH-secreting corticotroph pituitary adenoma (**Cushing disease**), the most common cause of endogenous Cushing syndrome.

(Choices A and B) Excess cortisol production due to an autonomously functioning adrenal adenoma,





## Exhibit Display

Features of Cushing syndrome Features of Cushing syndrome

Features of Cushing syndrome	
Clinical manifestations	<ul style="list-style-type: none"><li>• <b>Central obesity</b></li><li>• Skin atrophy &amp; wide, purplish <b>striae</b></li><li>• Proximal muscle weakness</li><li>• Hypertension</li><li>• <b>Glucose intolerance</b></li><li>• Skin hyperpigmentation (if due to ACTH excess)</li><li>• Depression, anxiety</li></ul>
Diagnosis	<ul style="list-style-type: none"><li>• <u>24-hour urinary cortisol excretion</u></li><li>• Late-night salivary cortisol assay</li><li>• Low-dose dexamethasone suppression test</li></ul>

This patient has well  
prominent features  
**dose dexamethasone**  
potent glucocorticoid  
endogenous Cushing

The most common  
basis of serum ACTH  
independent (ACTH  
**dexamethasone** sensitive  
secreting pituitary adenoma  
such as small cell lung

This patient has exogenous  
dexamethasone. This is  
**disease**), the most common

(Choices A and B)



New | Existing





dexamethasone. This is consistent with an ACTH-secreting corticotroph pituitary adenoma (Cushing disease), the most common cause of endogenous Cushing syndrome.

**(Choices A and B)** Excess cortisol production due to an autonomously functioning adrenal adenoma, adrenal carcinoma, or primary adrenocortical hyperplasia will cause Cushing syndrome with a suppressed ACTH level (ACTH independent). This patient's ACTH is elevated.

**(Choice C)** Administration of exogenous glucocorticoids is a common cause of Cushing syndrome. This is most common with systemic agents (eg, prednisone), but can occasionally be seen with topical or inhaled glucocorticoids. However, ACTH is suppressed in these cases.

### Educational objective:

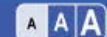
In Cushing syndrome due to an ACTH-secreting pituitary adenoma (Cushing disease), ACTH is high and cortisol production can be suppressed by high-dose, but not low-dose, dexamethasone. In patients with ectopic ACTH production (eg, from malignant tumors), cortisol and ACTH production are not suppressed by low- or high-dose dexamethasone.

### References

- [Cushing's disease.](#)







A 55-year-old woman, gravida 3 para 3, comes to the office due to constipation. For the past 6 months, the patient has had increasing constipation associated with mild, crampy abdominal pain and fatigue. She has only 1 or 2 bowel movements every week. Medical history is notable for nephrolithiasis, for which the patient was briefly hospitalized a year ago. She has not undergone colonoscopy. Vital signs are normal. The abdomen is soft. Rectal tone is normal. Deep tendon reflexes are 2+. The remainder of the examination shows no abnormalities. Laboratory results are as follows:

#### Serum chemistry

Sodium 140 mEq/L

Potassium 3.9 mEq/L

Creatinine 0.9 mg/dL

Calcium 11.5 mg/dL

Phosphorus (inorganic) 2.2 mg/dL

Which of the following is the most likely underlying cause of constipation in this patient?



A Decreased colonic smooth muscle contractility





Sodium	140 mEq/L
Potassium	3.9 mEq/L
Creatinine	0.9 mg/dL
Calcium	11.5 mg/dL
Phosphorus (inorganic)	2.2 mg/dL

Which of the following is the most likely underlying cause of constipation in this patient?

- ☐ A. Decreased colonic smooth muscle contractility
- ☐ B. Dysfunction of pelvic floor muscles
- ☐ C. Impaired sacral parasympathetic innervation
- ☐ D. Malignant obstruction of colon
- ☐ E. Segmental demyelination of autonomic nerves

Submit

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Sodium 140 mEq/L

Potassium 3.9 mEq/L

Creatinine 0.9 mg/dL

Calcium 11.5 mg/dL

Phosphorus (inorganic) 2.2 mg/dL

Which of the following is the most likely underlying cause of constipation in this patient?

- ☒ A. Decreased colonic smooth muscle contractility (68%)
- ☐ B. Dysfunction of pelvic floor muscles (6%)
- ☐ C. Impaired sacral parasympathetic innervation (8%)
- ☐ D. Malignant obstruction of colon (13%)
- ☐ E. Segmental demyelination of autonomic nerves (2%)







### Hypercalcemia-induced constipation

<b>Significant causes</b>	<ul style="list-style-type: none"><li>• Primary hyperparathyroidism</li><li>• Hypercalcemia of malignancy</li><li>• Vitamin D toxicity, milk-alkali syndrome</li></ul>
<b>Typical symptoms</b>	<ul style="list-style-type: none"><li>• Decreased frequency/increased hardness of stools</li><li>• Nausea, abdominal pain</li><li>• Nongastrointestinal symptoms: fatigue, polyuria, neuropsychiatric disturbance</li></ul>
<b>Pathophysiology</b>	<ul style="list-style-type: none"><li>• Inhibition of smooth muscle depolarization</li><li>• Decreased intestinal contractility/motility</li></ul>

This patient has **constipation** associated with **hypercalcemia** and hypophosphatemia, which is a common presentation of **primary hyperparathyroidism** (PHPT). PHPT is usually caused by a benign parathyroid adenoma that autonomously secretes parathyroid hormone (PTH), leading to increased bone resorption, increased renal calcium reabsorption, and increased intestinal calcium absorption (due to increased





This patient has **constipation** associated with **hypercalcemia** and hypophosphatemia, which is a common presentation of **primary hyperparathyroidism (PHPT)**. PHPT is usually caused by a benign parathyroid adenoma that autonomously secretes parathyroid hormone (PTH), leading to increased bone resorption, increased renal calcium reabsorption, and increased intestinal calcium absorption (due to increased production of 1,25-dihydroxyvitamin D). This patient's history of **renal stones** also indicates hyperparathyroidism and is due to increased urinary calcium excretion despite maximal renal tubular calcium reabsorption.

Hypercalcemia **inhibits nerve depolarization** by interfering with sodium movement through voltage-gated sodium channels, leading to **impaired smooth muscle contraction** and **reduced colonic motility**. Symptoms include constipation, crampy abdominal pain, and nausea. Other potential gastrointestinal manifestations of hypercalcemia include acute pancreatitis (due to increased conversion of trypsinogen to trypsin) and peptic ulcer (due to increased release of gastrin).

**(Choice B)** Dyssynergic defecation is characterized by altered passage of stool through the anorectum due to uncoordinated contraction and relaxation of pelvic floor muscles. It is often caused by obstetric complications during vaginal delivery. However, hypercalcemia and hypophosphatemia would not be present, and most patients have either anal sphincter dysfunction or the absence of perianal descent (this





due to uncoordinated contraction and relaxation of pelvic floor muscles. It is often caused by obstetric complications during vaginal delivery. However, hypercalcemia and hypophosphatemia would not be present, and most patients have either anal sphincter dysfunction or the absence of perianal descent (this patient's rectal tone is normal).

**(Choices C and E)** Intestinal motor function is generally stimulated by the parasympathetic nervous system and inhibited by the sympathetic nervous system. Although constipation can occur due to autonomic dysfunction from demyelination (eg, multiple sclerosis) or nerve fiber interruption (eg, traumatic spinal cord injury), these disorders would not explain this patient's electrolyte abnormalities.

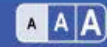
**(Choice D)** Colon cancer can cause intestinal obstruction, which can interfere with the passage of stool, and can be associated with hypercalcemia (bone metastasis); however, this would result in PTH suppression, so it is unlikely to cause hypophosphatemia. This patient's history of renal stones also is more consistent with primary hyperparathyroidism.

### Educational objective:

Hypercalcemia inhibits nerve depolarization, leading to impaired smooth muscle contraction and reduced colonic motility. Symptoms include constipation, crampy abdominal pain, and nausea.







A 4-week-old infant is evaluated for frequent episodes of hypoglycemia. The patient is found to have elevated insulin levels during periods of fasting. Several members of his family have a similar condition. Genetic testing reveals a mutation involving potassium channels expressed in pancreatic beta cells. The mutated channels have a higher sensitivity to the substance that normally modulates their activity, causing increased beta cell secretory activity. Which of the following substances normally binds to and regulates the ion channels that are responsible for this patient's hypoglycemia?

- ☐ A. ATP
- ☐ B. Citrate
- ☐ C. Fructose-6-phosphate
- ☐ D. Fumarate
- ☐ E. Glucose
- ☐ F. Lactate
- ☐ G. Malate
- ☐ H. Pyruvate





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- ☐ E. Glucose
- ☐ F. Lactate
- ☐ G. Malate
- ☐ H. Pyruvate





mutated channels have a higher sensitivity to the substance that normally modulates their activity, causing increased beta cell secretory activity. Which of the following substances normally binds to and regulates the ion channels that are responsible for this patient's hypoglycemia?

- ☒ A.ATP (68%)
- ☐ B.Citrate (2%)
- ☐ C.Fructose-6-phosphate (3%)
- ☐ D.Fumarate (0%)
- ☐ E.Glucose (22%)
- ☐ F.Lactate (0%)
- ☐ G.Malate (0%)
- ☐ H.Pyruvate (1%)

Correct



68%



43 secs



12/05/2020

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Feedback



Suspend



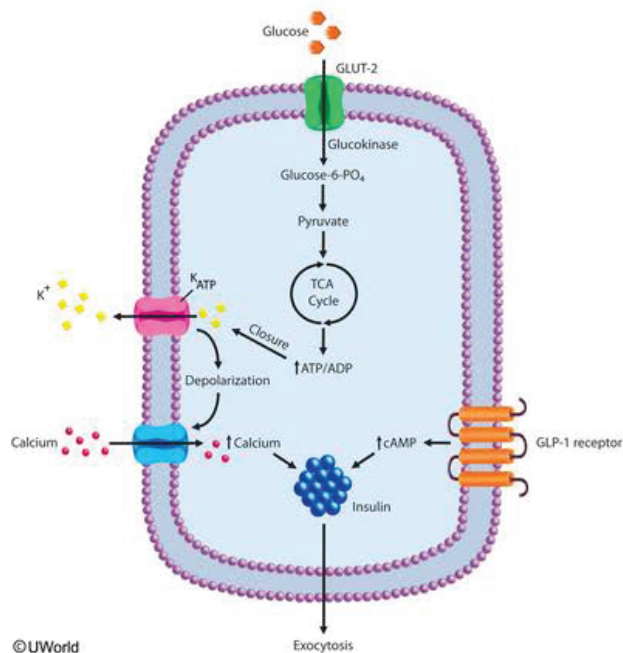
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## Exhibit Display

## Pancreatic beta cell function



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Exocytosis

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Pancreatic beta cells secrete insulin in response to elevated **glucose** levels. Glucose enters beta cells via **glucose transporter 2** (GLUT-2) and is metabolized via glycolysis and the citric acid cycle to generate **ATP**. ATP then binds to the regulatory subunit of the **ATP-sensitive potassium channel** ( $K_{ATP}$  channel).  $K_{ATP}$  channels are normally open at rest and maintain membrane polarization by allowing outward movement of potassium from the beta cells; however, on binding ATP, the  $K_{ATP}$  channels close. Increased intracellular ATP therefore leads to decreased potassium efflux and **membrane depolarization**. This triggers opening of voltage-dependent calcium channels, increased intracellular calcium levels, and subsequent **insulin release**.

Mutations in the  $K_{ATP}$  channel causing increased affinity for ATP result in fewer open channels and depolarization at lower glucose concentrations. This causes continued secretion of insulin despite falling blood glucose levels, leading to congenital hypoglycemia. Conversely, mutations of the  $K_{ATP}$  channels that decrease ATP affinity prevent appropriate depolarization in response to rising glucose levels, causing a familial form of neonatal diabetes mellitus. These patients can be treated successfully with sulfonylureas, which bind to  $K_{ATP}$  channels and cause closure independent of ATP.

**(Choices B, D, and G)** Citrate, fumarate, and malate are intermediate products in the citric acid cycle.





which bind to  $K_{ATP}$  channels and cause closure independent of ATP.

**(Choices B, D, and G)** Citrate, fumarate, and malate are intermediate products in the citric acid cycle.

During this process, energy is stored as NADH and  $FADH_2$ . ATP is then produced when NADH and  $FADH_2$  enter oxidative phosphorylation. However, these intermediates do not directly interact with  $K_{ATP}$  channels.

**(Choices C, F, and H)** Fructose-6-phosphate and pyruvate are products of the glycolytic pathway. Lactate is produced from pyruvate during anaerobic glycolysis. Glycolysis raises intracellular ATP levels, but these glycolytic intermediates do not act on  $K_{ATP}$  channels directly.

**(Choice E)** Glucose induces insulin release from beta cells via ATP formation but does not interact with  $K_{ATP}$  channels directly.

### Educational objective:

Oxidative metabolism of glucose in pancreatic beta cells generates ATP. ATP-induced closure of the ATP-sensitive potassium channels leads to membrane depolarization and subsequent insulin release.

### References

- [Hyperinsulinemic hypoglycemia.](https://pubmed.ncbi.nlm.nih.gov/26207052)







A 47-year-old woman comes to the office for follow up of an asthma exacerbation. The patient was recently hospitalized and required a prolonged period of mechanical ventilation as well as nebulized bronchodilators and intravenous glucocorticoids. Her symptoms improved, and she was discharged on oral prednisone. The patient reports compliance with therapy. She has no other medical conditions and takes no other medications. Blood pressure is 128/72 mm Hg, pulse is 85/min, and respirations are 18/min. On physical examination, there is mild expiratory wheezing. Because of the persistent respiratory findings, the patient is continued on the same treatment regimen. Long-term administration of this oral therapy is most likely to increase which of the following in this patient?

- ☐ A. Adrenocortical cell number
- ☐ B. Dermal collagen synthesis
- ☐ C. Expression of liver enzymes
- ☐ D. Lymphoid cell formation
- ☐ E. Muscle protein synthesis
- ☐ F. Osteoblastic bone formation





recently hospitalized and required a prolonged period of mechanical ventilation as well as nebulized bronchodilators and intravenous glucocorticoids. Her symptoms improved, and she was discharged on oral prednisone. The patient reports compliance with therapy. She has no other medical conditions and takes no other medications. Blood pressure is 128/72 mm Hg, pulse is 85/min, and respirations are 18/min. On physical examination, there is mild expiratory wheezing. Because of the persistent respiratory findings, the patient is continued on the same treatment regimen. Long-term administration of this oral therapy is most likely to **increase** which of the following in this patient?

- ☐ A. Adrenocortical cell number (11%)
- ☐ B. Dermal collagen synthesis (13%)
- ☒ C. Expression of liver enzymes (46%)
- ☐ D. Lymphoid cell formation (9%)
- ☐ E. Muscle protein synthesis (9%)
- ☐ F. Osteoblastic bone formation (10%)





### Effects of prolonged glucocorticoid therapy

<b>Adipose</b>	<ul style="list-style-type: none"><li>• Lipolysis</li><li>• Altered fat distribution</li></ul>
<b>Adrenal cortex</b>	<ul style="list-style-type: none"><li>• Atrophy</li></ul>
<b>Bone</b>	<ul style="list-style-type: none"><li>• Osteoporosis</li></ul>
<b>Immune system</b>	<ul style="list-style-type: none"><li>• Suppression</li><li>• T-cell apoptosis</li></ul>
<b>Liver</b>	<ul style="list-style-type: none"><li>• Increased gluconeogenesis &amp; glycogenesis</li></ul>
<b>Skeletal muscle</b>	<ul style="list-style-type: none"><li>• Atrophy (glucocorticoid myopathy)</li></ul>
<b>Skin</b>	<ul style="list-style-type: none"><li>• Thinning</li><li>• Stria</li><li>• Impaired wound healing</li></ul>

**Glucocorticoids** are potent stimulators of liver **gluconeogenesis** and unregulate the synthesis of key







**Glucocorticoids** are potent stimulators of liver **gluconeogenesis** and upregulate the synthesis of key gluconeogenic enzymes (eg, phosphoenolpyruvate carboxykinase, glucose-6-phosphatase).

Glucocorticoids also increase hepatic **glycogen** reserves by increasing expression of glycogen synthase, thereby improving glucose availability during periods of acute stress. The increased demand for metabolic enzymes required for these actions leads to an overall **increase in liver protein synthesis**.

Peripherally, glucocorticoids antagonize the actions of insulin in skeletal muscle, favoring **catabolism** and proteolysis to provide substrates for gluconeogenesis and glycogenesis in the liver (**Choice E**). This effect can manifest as proximal muscle weakness (glucocorticoid myopathy). The effect on adipose tissue is mixed, with lipolytic and antilipolytic effects, altered fat distribution (eg, central obesity, hypertrophy of the dorsocervical fat pad), and increased appetite and caloric intake. The net effect of gluconeogenesis and insulin antagonism is **hyperglycemia**.

**(Choice A)** Long-term glucocorticoid therapy causes atrophy of the adrenal cortex. On abrupt cessation, the delay in resumption of endogenous cortisol production can precipitate acute adrenal insufficiency.

**(Choice B)** Glucocorticoids inhibit fibroblast proliferation and collagen formation in the skin. This results in thinning of the skin, impaired wound healing, and **stria**. The connective tissue that supports the capillaries is also thinned, leading to easy bruising.





**(Choice B)** Glucocorticoids inhibit fibroblast proliferation and collagen formation in the skin. This results in thinning of the skin, impaired wound healing, and **stria**. The connective tissue that supports the capillaries is also thinned, leading to easy bruising.

**(Choice D)** Glucocorticoids are potent immunosuppressive agents. They increase expression of anti-inflammatory proteins but decrease expression of inflammatory proteins and cytokines and induce apoptosis in T cells (transient lymphopenia is common). Circulating neutrophil counts may increase in acute glucocorticoid administration due to increased release from bone marrow and "demargination" from peripheral tissues.

**(Choice F)** Glucocorticoids decrease bone mass by multiple mechanisms, including decreased gastrointestinal calcium absorption, increased renal calcium excretion, and direct inhibition of osteoblast activity.

### Educational objective:

Glucocorticoids are predominantly catabolic, causing muscle weakness, skin thinning, impaired wound healing, osteoporosis, and immunosuppression. However, they also cause increased hepatic synthesis of gluconeogenic and glycogenic proteins to increase glucose availability. This, along with peripheral antagonism of insulin, contributes to the development of hyperglycemia.





A 27-year-old woman in her 2nd trimester of pregnancy comes to the office due to constipation. Her stools have become increasingly hard and pellet-like over the past few weeks; bowel movements before then were always regular. She also has mild crampy abdominal pain and bloating, both of which improve after defecation. Medical history and family history are both unremarkable. This is the patient's first pregnancy and has so far been uncomplicated. On physical examination, the abdomen appears gravid but nontender. Which of the following best explains this patient's symptoms?

- ☐ A. Decreased colonic smooth muscle activity
- ☐ B. Decreased parasympathetic input to the colon
- ☐ C. Impaired relaxation of pelvic floor muscles
- ☐ D. Thickening of intestinal secretions
- ☐ E. Thinning of the rectovaginal septum

**Submit**





A 27-year-old woman in her 2nd trimester of pregnancy comes to the office due to constipation. Her stools have become increasingly hard and pellet-like over the past few weeks; bowel movements before then were always regular. She also has mild crampy abdominal pain and bloating, both of which improve after defecation. Medical history and family history are both unremarkable. This is the patient's first pregnancy and has so far been uncomplicated. On physical examination, the abdomen appears gravid but nontender. Which of the following best explains this patient's symptoms?

- ☒ A. Decreased colonic smooth muscle activity (36%)
- ☐ B. Decreased parasympathetic input to the colon (16%)
- ☐ C. Impaired relaxation of pelvic floor muscles (33%)
- ☐ D. Thickening of intestinal secretions (8%)
- ☐ E. Thinning of the rectovaginal septum (5%)

Correct

36%  
Answered correctly01 min, 10 secs  
Time Spent11/09/2020  
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### Common gastrointestinal adaptations in pregnancy

	Adaptation	Complication
<b>Esophagus</b>	<ul style="list-style-type: none"><li>• Progesterone decreases LES tone</li></ul>	<ul style="list-style-type: none"><li>• GERD</li></ul>
<b>Gallbladder</b>	<ul style="list-style-type: none"><li>• Estrogen increases cholesterol secretion into bile</li><li>• Progesterone reduces gallbladder motility</li></ul>	<ul style="list-style-type: none"><li>• Cholelithiasis</li><li>• Cholecystitis</li></ul>
<b>Intestines</b>	<ul style="list-style-type: none"><li>• Progesterone decreases colonic smooth muscle activity and decreases fasting MMCs in the small intestine</li><li>• Gravid uterus mechanically impedes small intestine transit</li></ul>	<ul style="list-style-type: none"><li>• Constipation</li><li>• Bloating</li><li>• Flatulence</li></ul>
<b>Rectum</b>	<ul style="list-style-type: none"><li>• Gravid uterus increases venous pressure</li></ul>	<ul style="list-style-type: none"><li>• Hemorrhoids</li></ul>

**LES** = lower esophageal sphincter; **GERD** = gastroesophageal reflux; **MMC** = migrating myoelectric complex.

Pregnancy has multiple effects in the gastrointestinal tract due to increasing levels of progesterone and estrogen as well as the effects of a gravid uterus on surrounding structures. **Constipation** is particularly common in pregnant patients and is largely due to the effects of **progesterone**, which has been shown





complex.

Pregnancy has multiple effects in the gastrointestinal tract due to increasing levels of progesterone and estrogen as well as the effects of a gravid uterus on surrounding structures. **Constipation** is particularly common in pregnant patients and is largely due to the effects of **progesterone**, which has been shown to **reduce colonic smooth muscle activity**. Progesterone also prevents the release of motilin, a hormone responsible for stimulating the fasting migrating myoelectric complex, which normally helps propel undigested food from the small intestines into the colon. Constipation may be exacerbated in later stages of pregnancy as the gravid uterus increases pressure on the small intestine, slowing intestinal transit.

Other common gastrointestinal alterations in pregnancy include reduced lower esophageal sphincter pressure (promoting gastroesophageal reflux) and gallbladder stasis (increasing the likelihood of developing gallstones). Hemorrhoids are also common and result from a rise in pressure within the rectal venous system due to the gravid uterus.

**(Choice B)** The parasympathetic nervous system stimulates peristalsis and gastrointestinal motility. Reduced parasympathetic input to the colon can lead to constipation; however, this typically occurs with neurologic disorders (eg, spinal cord injury, multiple sclerosis).

**(Choice C)** Defecatory dysfunction results from an inability to relax pelvic floor muscles, which prevents







**(Choice C)** Defecatory dysfunction results from an inability to relax pelvic floor muscles, which prevents proper evacuation of stool from the rectal vault. Although this can occur after trauma (eg, traumatic vaginal delivery), it is not a physiologic change that occurs during pregnancy.

**(Choice D)** Thickened intestinal secretions can cause constipation; however, this is typically seen in patients with cystic fibrosis, which affects water and electrolyte transportation. Patients with cystic fibrosis are typically diagnosed in infancy and have recurrent respiratory infections and failure to thrive.

**(Choice E)** Rectoceles occur when the rectum herniates into the vaginal canal through a thinned rectovaginal septum. Although they also cause constipation, rectoceles typically occur in elderly individuals with a history of multiple vaginal deliveries, not during pregnancy. Patients often report needing to manually compress the vagina to induce bowel movements.

### **Educational objective:**

Constipation is common during pregnancy and results from the inhibitory effect of progesterone on colonic smooth muscle contractions and the fasting migrating myoelectric complex. Other common pregnancy-related changes of the gastrointestinal system include decreased lower esophageal sphincter pressure (leading to gastroesophageal reflux) and gallbladder stasis (leading to gallstone formation).





Biochemists identify a mutation affecting the trypsinogen molecule that disrupts a critical site on the protein involved in inhibiting the active trypsin moiety. This mutation prevents trypsin from being permanently inactivated by enzymatic cleavage. Patients with this mutation would most likely suffer from which of the following conditions?

- ☐ A. Gastric cancer
- ☐ B. Liver cirrhosis
- ☐ C. Megaloblastic anemia
- ☐ D. Pancreatitis
- ☐ E. Peptic ulcer

Submit





Biochemists identify a mutation affecting the **trypsinogen** molecule that disrupts a critical site on the protein involved in inhibiting the active trypsin moiety. This mutation prevents trypsin from being permanently inactivated by enzymatic cleavage. Patients with this mutation would most likely suffer from which of the following conditions?

- ☐ A. Gastric cancer (1%)
- ☐ B. Liver cirrhosis (4%)
- ☐ C. Megaloblastic anemia (4%)
- ☒ D. Pancreatitis (77%)
- ☐ E. Peptic ulcer (11%)

Correct



77%

Answered correctly



45 secs

Time Spent



12/24/2020

Last Updated

Explanation

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**Pancreatic enzymes** (except amylase and lipase) are synthesized and secreted in inactive form to protect the pancreas from autodigestion. These proenzymes (zymogens) are then activated by trypsin in the duodenal lumen after trypsinogen is converted into its active form, **trypsin**, by the action of duodenal enterokinase. Trypsin can also activate other trypsinogen molecules; therefore, even small amounts of it can result in an **activation cascade**. Because of trypsin's central role in the activation of pancreatic digestive proenzymes, multiple protective mechanisms exist to limit the amount of trypsinogen that becomes prematurely activated:

- Serine peptidase inhibitor Kazal-type 1 (**SPINK1**) is secreted by pancreatic acinar cells and functions as a **trypsin inhibitor**. It impedes the activity of trypsinogen molecules that become prematurely activated within the pancreas.
- In addition to functioning as its own activator, trypsin can serve as its own inhibitor by cleaving active trypsin molecules at a second site, rendering them inactive.

**Hereditary pancreatitis** is a rare disorder that results from mutations involving the trypsinogen or *SPINK1* gene. The most common mutation leads to the production of **abnormal trypsin** that is not susceptible to **inactivating cleavage** by trypsin. Because a small amount of trypsinogen normally activates prematurely within the pancreatic acini and ducts, these protective mechanisms are critical for preventing recurrent attacks of acute pancreatitis.





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Tutorial

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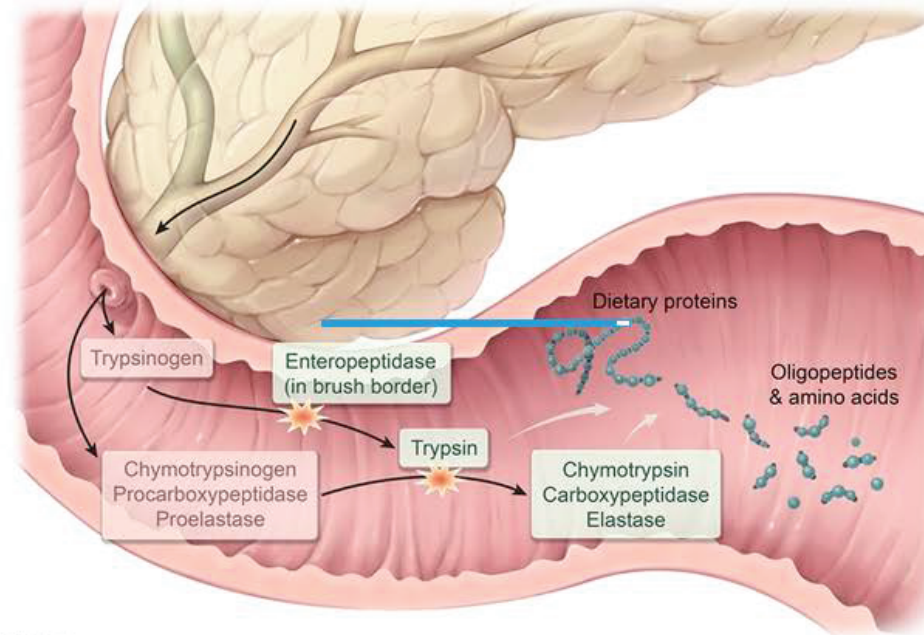
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## Exhibit Display

## Pancreatic enzyme activation



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attacks of acute pancreatitis.

**(Choices A and E)** Peptic ulcer disease and gastric adenocarcinoma are strongly associated with *Helicobacter pylori* infection.

**(Choice B)** Patients with mutations affecting the serum protease inhibitor, alpha-1-antitrypsin, can have emphysema and liver cirrhosis. However, there is no association between cirrhosis and trypsinogen gene mutations.

**(Choice C)** Megaloblastic anemia is due to deficiencies of vitamin B<sub>12</sub> and folate. It is also associated with a number of drugs (eg, methotrexate, phenytoin) and certain inborn metabolic errors.

### Educational objective:

Multiple inhibitory mechanisms exist to prevent premature activation of trypsinogen before it reaches the duodenal lumen, including cleavage inactivation of trypsin by trypsin itself and production of trypsin inhibitors (eg, SPINK1). Gene mutations that render trypsin insensitive to cleavage inactivation cause hereditary pancreatitis.

Pathophysiology

Gastrointestinal & Nutrition

Acute pancreatitis

Subject

System

Topic







A 79-year-old woman is brought to the emergency department from the nursing home due to explosive diarrhea. Laboratory studies show leukocytosis, and results from a stool specimen return positive for *Clostridium difficile* toxin genes by polymerase chain reaction. Three days later, one of the nurses who cared for the patient at the nursing home is admitted with diarrhea and is found to have *C difficile* infection. However, the other nurses who also took care of the patient are asymptomatic and do not develop the infection. If all the nurses were similarly exposed to *C difficile*, which of the following is the most likely reason that the asymptomatic nurses did not develop the infection?

- ☐ A. Adequate pancreatic enzyme secretion
- ☐ B. Intact cell-mediated immunity
- ☐ C. Preformed antispore immunoglobulins
- ☐ D. Preserved intestinal microbiome
- ☐ E. Rapid gastrointestinal transit and expulsion of spores

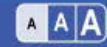
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- ☐ A. Adequate pancreatic enzyme secretion (0%)
- ☐ B. Intact cell-mediated immunity (5%)
- ☐ C. Preformed antispore immunoglobulins (5%)
- ☒ D. Preserved intestinal microbiome (84%)
- ☐ E. Rapid gastrointestinal transit and expulsion of spores (4%)





Over 400 types of bacteria inhabit the healthy human gastrointestinal tract as part of the normal **intestinal microbiome**. In healthy humans, these include very few aerobes (eg, *Pseudomonas*), approximately 10% facultative anaerobes (eg, *Escherichia coli*, *Klebsiella*, *Lactobacillus*, *Bacillus*), and a majority of strict anaerobes (eg, *Bacteroides*, *Fusobacterium*, *Clostridium*). These intestinal bacteria effectively **suppress overgrowth of *Clostridium difficile*** and other potentially pathogenic bacteria by competing for nutrients and adhesion sites within the gut.

**Antibiotic therapy** is the most important risk factor for *C difficile* infection (CDI) as it can alter the microbiome, leading to a potential overgrowth of pathogenic strains and clinical disease. The organism causes disease by releasing 2 toxins that damage the mucosal lining of the large intestine, leading to diarrhea (toxin A) and necrosis (toxin B) with pseudomembrane formation.

**(Choice A)** Increased risk of CDI is seen with proton pump inhibitor use, suggesting that gastric acidity may have a protective role. The pancreas secretes protease, amylase and lipase, and trypsinogen, among others; however, there is no association between pancreatic enzyme secretion and CDI.

**(Choice B)** Cell-mediated immunity is not essential for prevention of CDI, but it is required to eradicate infections with intracellular agents that avoid the humoral (antibody) immune response (eg, *Legionella*,







may have a protective role. The pancreas secretes protease, amylase and lipase, and trypsinogen, among others; however, there is no association between pancreatic enzyme secretion and CDI.

**(Choice B)** Cell-mediated immunity is not essential for prevention of CDI, but it is required to eradicate infections with intracellular agents that avoid the humoral (antibody) immune response (eg, *Legionella*, *Neisseria gonorrhoeae*, *Listeria monocytogenes*, viruses, *Leishmania*).

**(Choice C)** Individuals usually develop serum antibodies against *C difficile* toxins, not spores.

**(Choice E)** Rapid gastrointestinal transit is rarely effective at "washing away" pathogenic diarrhea-causing organisms as they are well-adapted to adhering to the gut mucosa in the setting of voluminous diarrhea.

### Educational objective:

In the absence of normal intestinal microbial flora (as may be the case after a course of antibiotics), *Clostridium difficile* can overgrow and produce enterotoxin (toxin A) and cytotoxin (toxin B). Clinical disease resulting from *C difficile* overgrowth can range from transient diarrhea to severe pseudomembranous colitis.

### References

- [The host immune response to Clostridium difficile infection.](#)





A 72-year-old man comes to the office due to watery diarrhea and abdominal cramps. The symptoms began several days after he started chemotherapy for metastatic colon cancer. He denies hematochezia, melena, or bulky, foul-smelling stools. Vital signs are within normal limits, and physical examination is unremarkable. Laboratory testing reveals no electrolyte abnormalities and no leukocytosis. Stool testing is negative for infection and fecal occult blood. The patient is advised to take a medication after each loose stool. The medication works by inhibiting the release of acetylcholine in the intestinal wall but does not cross the blood-brain barrier. Which of the following is the most likely medication prescribed for this patient?

- ☐ A. Aprepitant
- ☐ B. Bismuth subsalicylate
- ☐ C. Fentanyl
- ☐ D. Loperamide
- ☐ E. Neostigmine
- ☐ F. Octreotide



began several days after he started chemotherapy for metastatic colon cancer. He denies hematochezia, melena, or bulky, foul-smelling stools. Vital signs are within normal limits, and physical examination is unremarkable. Laboratory testing reveals no electrolyte abnormalities and no leukocytosis. Stool testing is negative for infection and fecal occult blood. The patient is advised to take a medication after each loose stool. The medication works by inhibiting the release of acetylcholine in the intestinal wall but does not cross the blood-brain barrier. Which of the following is the most likely medication prescribed for this patient?

- ☐ A. Aprepitant (8%)
- ☐ B. Bismuth subsalicylate (5%)
- ☐ C. Fentanyl (1%)
- ☒ D. Loperamide (51%)
- ☐ E. Neostigmine (18%)
- ☐ F. Octreotide (14%)





## Antidiarrheal agents

### Opioid agonists

(eg, loperamide, diphenoxylate with atropine, tincture of opium)

- Binds to mu opiate receptors in the colonic myenteric plexus, slowing peristalsis

### Bulk forming agents

(eg, psyllium, pectin)

- Absorbs water and intraluminal contents to form stool

### Bismuth subsalicylate

- Stimulates intestinal fluid absorption and inhibits prostaglandin synthesis (antispasmodic effect)

### Octreotide

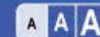
- Somatostatin analog that reduces secretion of pancreatic and GI hormones

### Bile acid sequestrants

(eg, cholestyramine)

- Binds bile acid in intestines (used for bile-acid diarrhea)





This patient with uncomplicated, chemotherapy-induced diarrhea was prescribed **loperamide**. Loperamide is an **opioid agonist** that exerts its antidiarrheal effects by binding to **mu opiate receptors** in the colonic myenteric plexus. This **inhibits acetylcholine release** from myenteric plexus neurons, decreasing activity of the intestinal smooth muscles and **slowing peristalsis**. Transit time within the intestine is prolonged, allowing for increased water absorption. In addition, the anticholinergic effects also result in decreased secretion from the intestinal epithelia, further reducing stool volume and increasing fecal consistency.

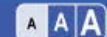
Unlike other opiates (eg, hydrocodone, fentanyl), loperamide undergoes **high first-pass metabolism** and **does not cross the blood-brain barrier**, allowing it to be used without opiate-related adverse events (eg, respiratory depression, sedation) or threat of abuse. The only side effect is constipation, which can be avoided with careful dose titration. Diphenoxylate, another opiate used for diarrhea, is less extensively metabolized and crosses the blood-brain barrier. To discourage abuse, diphenoxylate is typically combined with a small amount of atropine, an anticholinergic medication that results in dry mouth, flushing, pupil dilation, and urinary retention when used in large amounts.

**(Choice A)** Aprepitant is a neurokinin-1 receptor antagonist used for chemotherapy-related nausea and vomiting, not diarrhea.

**(Choice B)** Bismuth subsalicylate is frequently used for diarrhea and dyspepsia. Although its mechanism







**(Choice B)** Bismuth subsalicylate is frequently used for diarrhea and dyspepsia. Although its mechanism of action is not clearly understood, it stimulates the intestinal absorption of fluid (reducing diarrhea) and inhibits prostaglandin synthesis (reducing hypermotility). It does not inhibit acetylcholine release.

**(Choice C)** Fentanyl is an opiate commonly used as an analgesic and sedative. Although it causes constipation, it crosses the blood-brain barrier and therefore is not used for diarrhea due to the risk of systemic opiate-related adverse events (eg, respiratory depression, abuse).

**(Choice E)** Neostigmine is an acetylcholinesterase inhibitor that increases acetylcholine within the synapse. Its cholinergic effects would worsen this patient's diarrhea.

**(Choice F)** Octreotide is a somatostatin analogue that is sometimes used for refractory chemotherapy-induced diarrhea; however, it exerts its antidiarrheal effect by reducing secretion of pancreatic and gastrointestinal hormones (eg, secretin, gastrin, vasoactive intestinal peptide).

### **Educational objective:**

Loperamide is an opioid agonist that exerts its antidiarrheal effects by binding to mu opiate receptors in the colonic myenteric plexus, which inhibits acetylcholine release, decreases intestinal smooth muscle activity, and slows peristalsis. It undergoes high first-pass metabolism and does not cross the blood-brain barrier, thus avoiding systemic opiate-related adverse events (eg, sedation, respiratory depression).







A 65-year-old woman comes to the office after finding blood in her stool. She is physically active and exercises regularly. She does not use tobacco or alcohol. She has no history of peptic ulcer disease. Her physical examination is unremarkable. Colonoscopy reveals several large adenomatous polyps with severe dysplasia in the sigmoid colon. She undergoes resection of the sigmoid colon, and her carcinoembryonic antigen level is normal. The patient is interested in decreasing her chances of developing new polyps and colon cancer. The physician discusses exercise, healthy weight, and dietary factors associated with reduction of colon cancer risk, including increased fiber intake and reduced consumption of refined sugars and fat. Which of the following enzymes could be inhibited with medication to further reduce this patient's risk of developing recurrent adenoma?

- ☐ A. Angiotensin-converting enzyme
- ☐ B. Caspase
- ☐ C. Cyclooxygenase-2
- ☐ D. Glutamate dehydrogenase
- ☐ E. Phenylalanine hydroxylase





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- ☐ F. Xanthine oxidase





severe dysplasia in the sigmoid colon. She undergoes resection of the sigmoid colon, and her carcinoembryonic antigen level is normal. The patient is interested in decreasing her chances of developing new polyps and colon cancer. The physician discusses exercise, healthy weight, and dietary factors associated with reduction of colon cancer risk, including increased fiber intake and reduced consumption of refined sugars and fat. Which of the following enzymes could be inhibited with medication to further reduce this patient's risk of developing recurrent adenoma?

- ☐ A. Angiotensin-converting enzyme (2%)
- ☐ B. Caspase (11%)
- ☒ C. Cyclooxygenase-2 (60%)
- ☐ D. Glutamate dehydrogenase (13%)
- ☐ E. Phenylalanine hydroxylase (4%)
- ☐ F. Xanthine oxidase (8%)

Correct



60%

Answered correctly



01 min, 11 secs

Time spent



01/18/2021

Last updated

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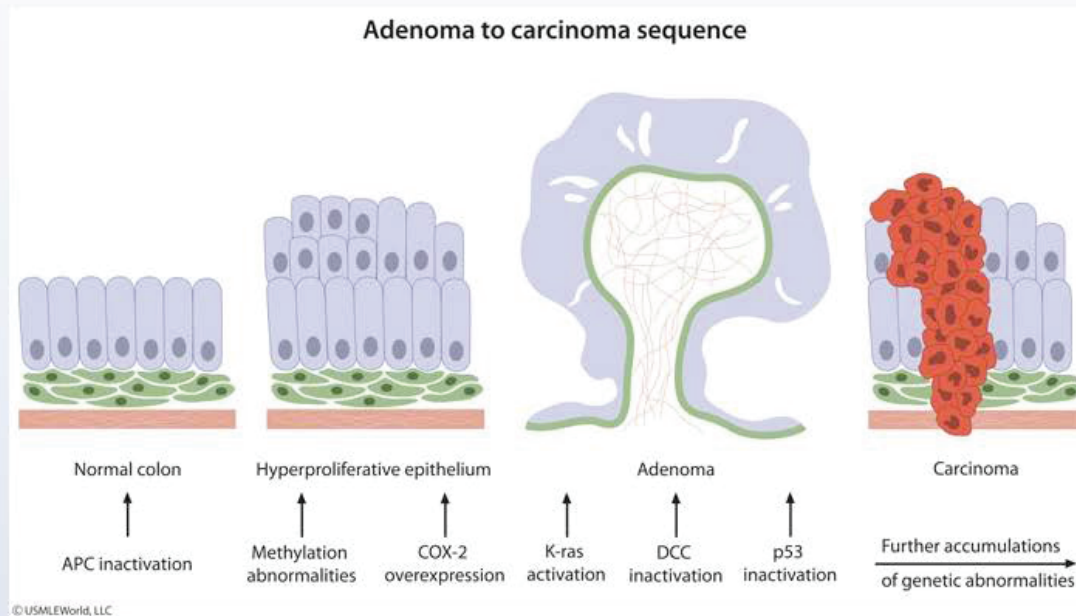


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## Explanation



**Adenomatous polyps** contain dysplastic mucosa and are premalignant. They tend to develop in patients age >50 as a result of mutations in the *APC* tumor suppressor gene, which regulates cell growth and





**Adenomatous polyps** contain dysplastic mucosa and are premalignant. They tend to develop in patients age >50 as a result of mutations in the *APC* tumor suppressor gene, which regulates cell growth and adhesion. Progression to adenocarcinoma proceeds as other mutations occur in genes such as *KRAS* and *TP53*. This accumulation of gene mutations is called the "**adenoma-to-carcinoma sequence**."

Increased activity of the enzyme **cyclooxygenase-2** (COX-2) has been found in many forms of colon adenocarcinoma and in inherited polyposis syndromes. This may be due to the need for COX-induced prostaglandin production, which leads to epithelial proliferation. Regular **aspirin** (a COX inhibitor) intake has been associated with lower rates of colonic adenoma and adenocarcinoma, although this must be balanced against bleeding risk.

**(Choice A)** Angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II, which plays an important role in hypertension and congestive heart failure. ACE inhibitors are widely used to treat these conditions.

**(Choice B)** Caspases are cysteine proteases that are an essential component in cellular apoptosis. Inhibition of caspase activity would lead to cells that are resistant to apoptosis; this is one of the mechanisms involved in the progression of the adenoma-to-carcinoma sequence.





conditions.

**(Choice B)** Caspases are cysteine proteases that are an essential component in cellular apoptosis.

Inhibition of caspase activity would lead to cells that are resistant to apoptosis; this is one of the mechanisms involved in the progression of the adenoma-to-carcinoma sequence.

**(Choices D and E)** Glutamate dehydrogenase (produces ammonia for use in the urea cycle) and phenylalanine hydroxylase (converts phenylalanine to tyrosine) have not been implicated in the development of adenomatous polyps.

**(Choice F)** Xanthine oxidase is an enzyme that participates in uric acid synthesis. Allopurinol is a xanthine oxidase inhibitor used to lower serum levels of uric acid in gout and tumor lysis syndrome.

### Educational objective:

Adenomatous polyps contain dysplastic mucosa and are premalignant. Regular screening with timely excision of polyps is effective for prevention of colon adenocarcinoma. Studies have linked increased activity of cyclooxygenase-2 to some forms of colon adenocarcinoma and suggest that regular aspirin use decreases adenomatous polyp formation.

### References

- Cyclooxygenase-2 overexpression is common in serrated and non-serrated colorectal adenoma, but







A 3-year-old boy is brought to the emergency department by his parents after he develops acute abdominal pain and vomiting. Imaging studies reveal a foreign body lodged within his intestine causing a small bowel obstruction. Laparotomy is performed to remove the foreign body; during the procedure, an incidental abdominal cyst is discovered and removed. The cyst is connected by a fibrous band to the ileum and the umbilicus. Which of the following conditions is also caused by the same embryologic defect responsible for this patient's abdominal cyst?

- ☐ A. Duodenal atresia
- ☐ B. Hirschsprung disease
- ☐ C. Meckel diverticulum
- ☐ D. Umbilical hernia
- ☐ E. Imperforate anus
- ☐ F. Omphalocele
- ☐ G. Malrotation





pain and vomiting. Imaging studies reveal a foreign body lodged within his intestine causing a small bowel obstruction. Laparotomy is performed to remove the foreign body; during the procedure, an incidental abdominal cyst is discovered and removed. The cyst is connected by a fibrous band to the ileum and the umbilicus. Which of the following conditions is also caused by the same embryologic defect responsible for this patient's abdominal cyst?

- ☐ A. Duodenal atresia (1%)
- ☐ B. Hirschsprung disease (0%)
- ☒ C. Meckel diverticulum (79%)
- ☐ D. Umbilical hernia (5%)
- ☐ E. Imperforate anus (1%)
- ☐ F. Omphalocele (8%)
- ☐ G. Malrotation (2%)

Correct

79%



34 secs



11/10/2020

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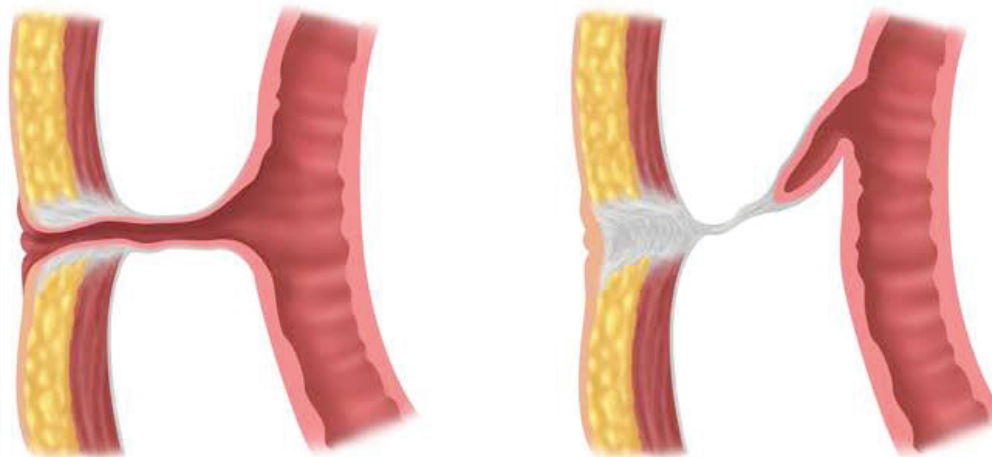
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## Vitelline duct abnormalities



Persistent vitelline duct

Meckel diverticulum

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The omphalomesenteric (vitelline) duct connects the midgut lumen with the yolk sac cavity early in embryonic life. It normally obliterates during the 7<sup>th</sup> week of embryonic development. If its obliteration is incomplete or abnormal, a number of abnormalities can result:







The omphalomesenteric (vitelline) duct connects the midgut lumen with the yolk sac cavity early in embryonic life. It normally obliterates during the 7<sup>th</sup> week of embryonic development. If its obliteration is incomplete or abnormal, a number of abnormalities can result:

1. A **persistent vitelline duct**, or vitelline fistula, occurs due to complete failure of the vitelline duct to close. A small connection between the intestinal lumen and the outside of the body exists at the umbilicus. Meconium discharge from the umbilicus is seen soon after birth if such a fistula is present.
2. **Meckel diverticulum** is the most common vitelline duct anomaly. It results from a partial closure of the vitelline duct, with the patent portion attached to the ileum. A fibrous band may connect the tip of the Meckel diverticulum with the umbilicus.
3. **Vitelline sinus** results from a partial closure of the vitelline duct, with the patent portion open at the umbilicus.
4. **Vitelline duct cyst** (enterocyst) forms if peripheral portions of the vitelline duct (connected to the ileum and umbilicus) obliterate, but the central part remains. This cyst is connected with the ileum and abdominal wall by fibrous bands.

Most vitelline duct abnormalities are asymptomatic and often discovered incidentally. However, Meckel diverticulum may present with rectal bleeding or intestinal obstruction. Remember the rule of 2's with Meckel diverticulum: 2% of the population, 2 feet from the ileocecal valve, 2 inches in length, 2% are





Most vitelline duct abnormalities are asymptomatic and often discovered incidentally. However, Meckel diverticulum may present with rectal bleeding or intestinal obstruction. Remember the rule of 2's with Meckel diverticulum: 2% of the population, 2 feet from the ileocecal valve, 2 inches in length, 2% are symptomatic, and males are 2 times more likely to be affected.

**(Choice A)** Duodenal atresia results from failure of the duodenum to recanalize in early embryonic life. Although often associated with trisomy 21, it is not associated with any vitelline duct anomalies.

**(Choice B)** Hirschsprung disease results from the failure of migration of neural crest cells into the intestinal wall.

**(Choice D)** Umbilical hernias occur due to weakness of the abdominal wall at the umbilicus. These hernias are common in children and usually close spontaneously by 2 years of age. Unlike omphaloceles, umbilical hernias are midline protrusions that are covered by skin.

**(Choice E)** Imperforate anus occurs due to abnormal development of anorectal structures. This condition manifests during the first days of life, when the newborn fails to pass meconium.

**(Choice F)** Omphalocele is a midline defect in the abdominal wall due to incomplete closure during fetal life. Abdominal organs protrude through the defect, covered with a peritoneal sac.







Intestinal wall.

**(Choice D)** Umbilical hernias occur due to weakness of the abdominal wall at the umbilicus. These hernias are common in children and usually close spontaneously by 2 years of age. Unlike omphaloceles, umbilical hernias are midline protrusions that are covered by skin.

**(Choice E)** Imperforate anus occurs due to abnormal development of anorectal structures. This condition manifests during the first days of life, when the newborn fails to pass meconium.

**(Choice F)** Omphalocele is a midline defect in the abdominal wall due to incomplete closure during fetal life. Abdominal organs protrude through the defect, covered with a peritoneal sac.

**(Choice G)** Malrotation results from the failure of the midgut to rotate counterclockwise as it returns to the abdominal cavity during early embryonic development. Malrotation leads to abnormal positioning of the intestine in the abdominal cavity and sometimes twisting of an intestinal loop (volvulus).

### Educational objective:

The omphalomesenteric (vitelline) duct normally obliterates during the 7<sup>th</sup> week of embryonic development. Both enterocysts and Meckel diverticula result from a failure of obliteration involving the omphalomesenteric duct.

### References







A 46-year-old man comes to the physician complaining of intermittent, bloody diarrhea and abdominal pain for the past month. He has lost 12 lbs (5.5 kg) during this period. He was diagnosed with HIV five years ago, but has been noncompliant with his antiretroviral medications. Laboratory results show a CD4 count of 50 cells/ $\mu$ L and viral load of 650,000 copies/mL. Colonoscopy reveals multiple hemorrhagic polypoidal lesions. Biopsy of these lesions reveals spindle cells with surrounding blood vessel proliferation. Which of the following is the most likely cause of this patient's diarrhea?

- ☐ A. Adenocarcinoma
- ☐ B. Cytomegalovirus
- ☐ C. Cryptosporidium
- ☐ D. Entamoeba histolytica
- ☐ E. Kaposi's sarcoma
- ☐ F. Ulcerative colitis

**Submit**

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Feedback



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End Block



A 46-year-old man comes to the physician complaining of intermittent, bloody diarrhea and abdominal pain for the past month. He has lost 12 lbs (5.5 kg) during this period. He was diagnosed with HIV five years ago, but has been noncompliant with his antiretroviral medications. Laboratory results show a CD4 count of 50 cells/ $\mu$ L and viral load of 650,000 copies/mL. Colonoscopy reveals multiple hemorrhagic polypoidal lesions. Biopsy of these lesions reveals spindle cells with surrounding blood vessel proliferation. Which of the following is the most likely cause of this patient's diarrhea?

- ☐ A. Adenocarcinoma (9%)
- ☐ B. Cytomegalovirus (11%)
- ☐ C. Cryptosporidium (21%)
- ☐ D. Entamoeba histolytica (5%)
- ☒ E. Kaposi's sarcoma (48%)
- ☐ F. Ulcerative colitis (3%)



**Colonic manifestations of various diseases**

Disease	Colonoscopy findings	Biopsy findings
Adenocarcinoma	Usually a protuberant mass	Dysplastic mucosal cells with variable degree of gland formation
Cytomegalovirus	Multiple ulcers and mucosal erosions	Cytomegalic cells with inclusion bodies
Cryptosporidium	Nonulcerative inflammation	Basophilic clusters seen on the surface of intestinal mucosal cells
Entamoeba histolytica	Numerous discrete, flask-shaped ulcerative lesions	Trophozoites containing red blood cells
Kaposi's	Reddish/violet, flat	Spindle-shaped tumor







	mucosal erosions	Inclusion bodies
Cryptosporidium	Nonulcerative inflammation	Basophilic clusters seen on the surface of intestinal mucosal cells
Entamoeba histolytica	Numerous discrete, flask-shaped ulcerative lesions	Trophozoites containing red blood cells
Kaposi's sarcoma	Reddish/violet, flat maculopapular lesions or hemorrhagic nodules	Spindle-shaped tumor cells with small-vessel proliferation
Ulcerative colitis	Contiguous area of erythematous, friable, granular mucosa with possible pseudopolyps	Inflammatory infiltrate involving the mucosa and submucosa with crypt abscesses

Causes of diarrhea in HIV patients include opportunistic and non-opportunistic infections as well as noninfectious causes such as Kaposi's sarcoma (KS). KS is a vascular malignancy caused by human





possible pseudopolyps

crypt abscesses

Causes of diarrhea in HIV patients include opportunistic and non-opportunistic infections as well as noninfectious causes such as Kaposi's sarcoma (KS). KS is a vascular malignancy caused by human herpesvirus 8 (HHV-8). HIV co-infection substantially increases the risk for developing KS. Skin involvement is characteristic, but extracutaneous spread of KS to the lungs and gastrointestinal tract is also common.

KS lesions are easily distinguished endoscopically. They vary from reddish/violet flat maculopapular lesions to raised hemorrhagic nodules or polypoid masses. On biopsy, **KS lesions** will typically show spindle cells with cytologic atypia, blood vessel proliferation, and extravasated red blood cells with hemosiderin deposition.

**(Choice A)** **Adenocarcinoma** typically would show dysplastic mucosal cells with a variable degree of gland formation, depending on the differentiation of the tumor.

**(Choice B)** Colonoscopy in cytomegalovirus colitis would show multiple ulcers and mucosal erosions. Biopsy shows characteristic **cytomegalic cells** with inclusion bodies.

**(Choice C)** Cryptosporidiosis can cause profuse, watery, nonbloody diarrhea, particularly in patients with advanced AIDS (CD4 counts  $< 180$  cells/mm<sup>3</sup>). Endoscopy shows inflammation but no ulcers. Biopsy





Item 7 of 40

Question Id: 8290



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Previous



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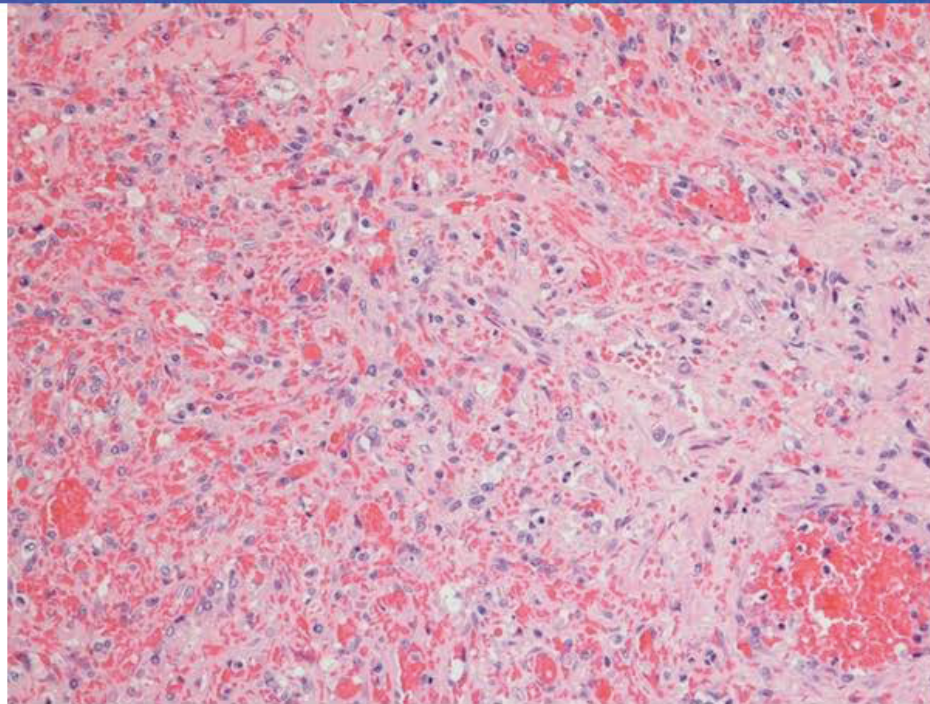
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possible pseudopolyps crypt abscesses

Exhibit Display



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advanced AIDS (CD4 counts < 160 cells/mm<sup>3</sup>). Endoscopy shows inflammation but no ulcers. Biopsy

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Item 7 of 40

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Calculator



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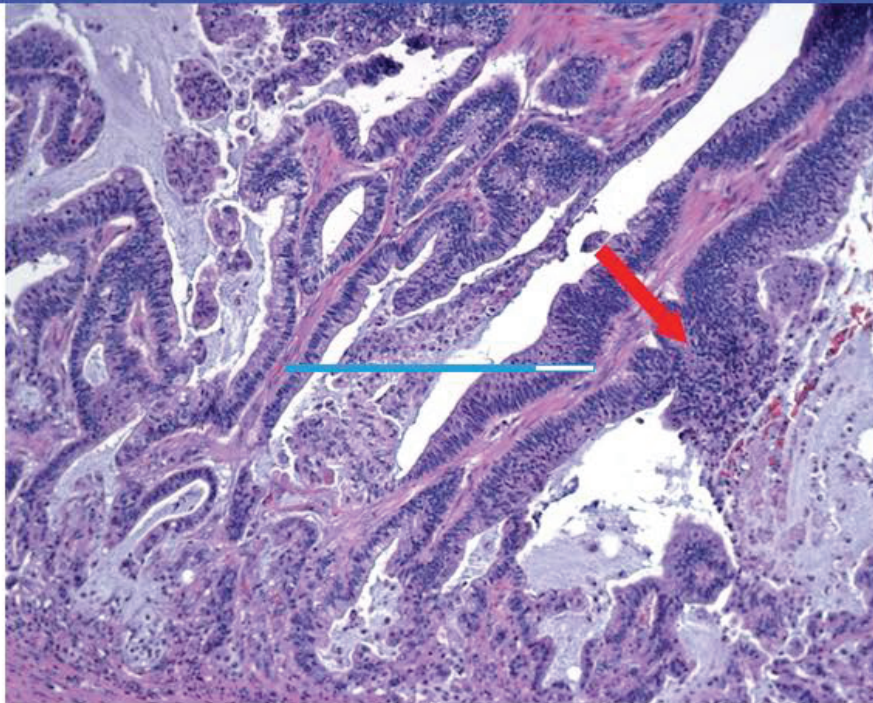
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advanced AIDS (CD4 counts < 160 cells/mm<sup>3</sup>). Endoscopy shows inflammation but no ulcers. Biopsy

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Item 7 of 40

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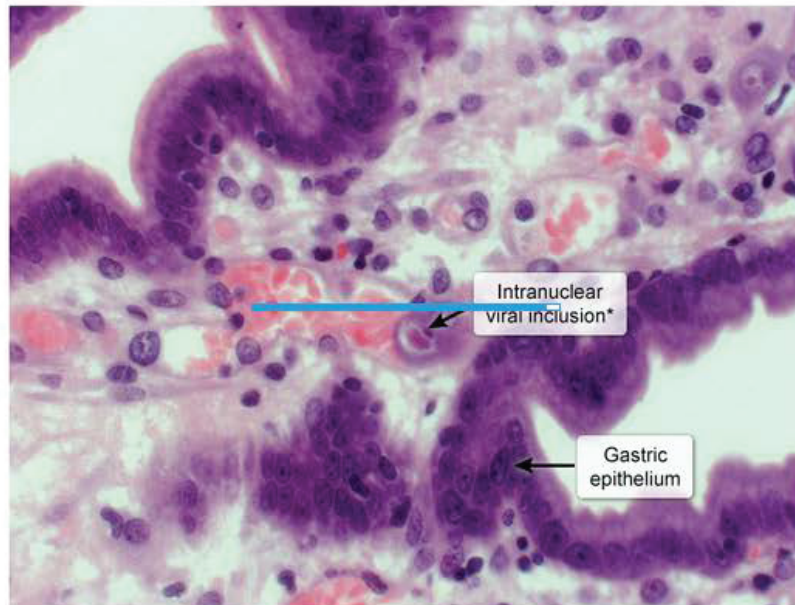
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possible pseudopolyps | crypt abscesses

Exhibit Display

### Cytomegalovirus



\*\*"Owl's eye" appearance

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advanced AIDS (CD4 counts < 100 cells/mm<sup>3</sup>). Endoscopy shows inflammation but no ulcers. Biopsy

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Biopsy shows characteristic **cytomegalic cells** with inclusion bodies.

**(Choice C)** Cryptosporidiosis can cause profuse, watery, nonbloody diarrhea, particularly in patients with advanced AIDS (CD4 counts < 180 cells/mm<sup>3</sup>). Endoscopy shows inflammation but no ulcers. Biopsy shows **basophilic clusters** on the surface of intestinal mucosal cells.

**(Choice D)** Entamoeba histolytica can cause bloody diarrhea and liver abscess formation. Colonoscopy would show the presence of flask-shaped colonic ulcers.

**(Choice F)** Colonoscopy in ulcerative colitis would show erythematous, friable, granular mucosa and possibly pseudopolyps (isolated areas of regenerative mucosa). An inflammatory infiltrate involving the mucosa and submucosa with **crypt abscesses** would be seen histologically.

### Educational objective:

Kaposi's sarcoma usually involves the skin and GI tract and is common in HIV patients not on antiretroviral therapy. Endoscopy reveals characteristic lesions, which range from reddish/violet flat maculopapular lesions to raised hemorrhagic nodules or polypoid masses. Biopsy can show spindle cells, neovascularization, and extravasated red blood cells.

### References

- [Gastrointestinal malignancies in HIV-infected or immunosuppressed patients: pathologic features and](#)





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Previous

Next

Full Screen

Tutorial

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Notes

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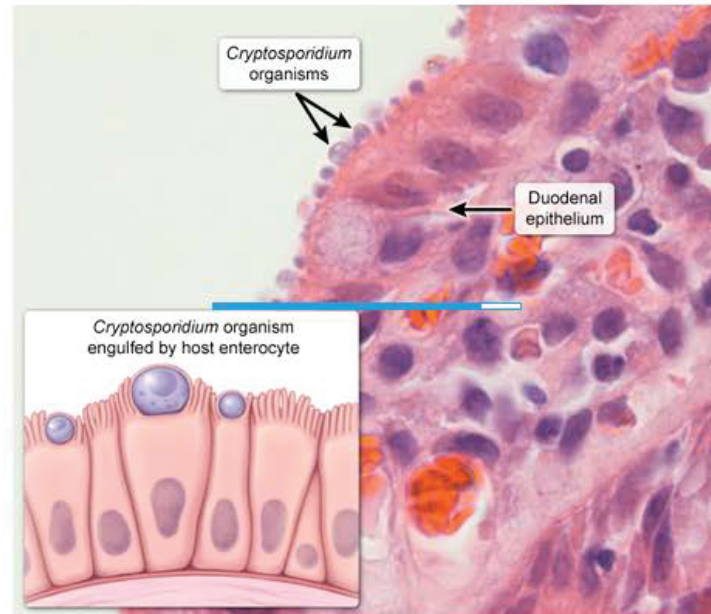
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Biopsy shows characteristic cytomegalic cells with inclusion bodies.

## Exhibit Display

## Cryptosporidiosis



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Item 7 of 40

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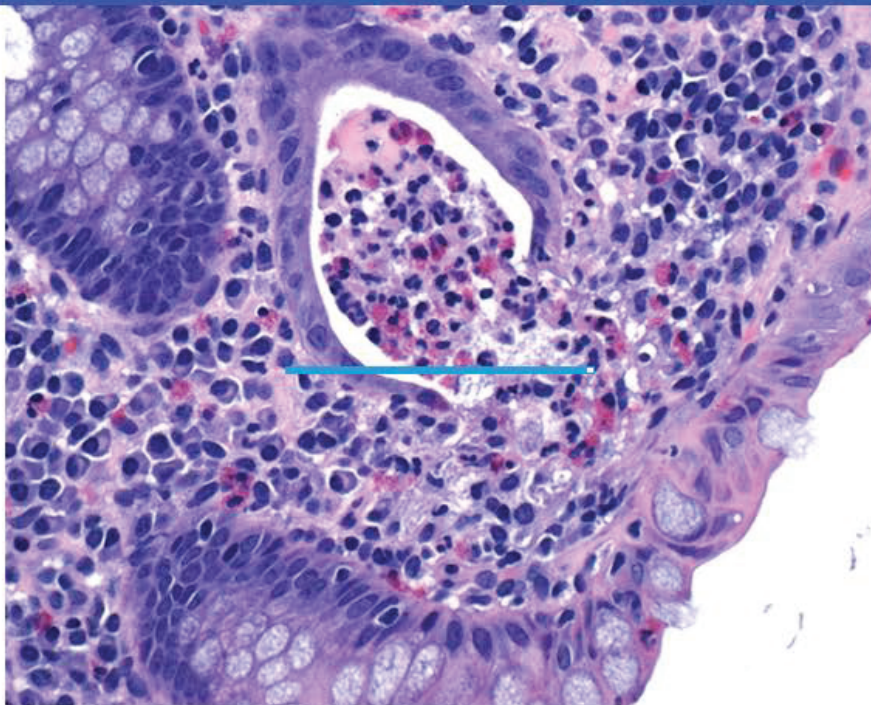
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Biopsy shows characteristic cytomegalic cells with inclusion bodies.

Exhibit Display



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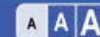
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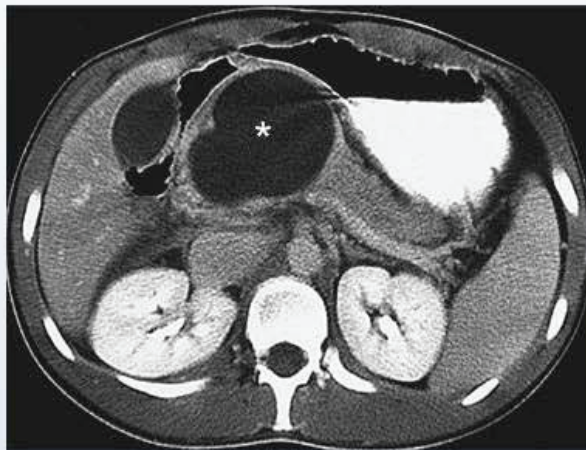
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A 48-year-old male is admitted to the hospital with severe epigastric abdominal pain and vomiting after an episode of binge-drinking. Four weeks later, he is found to have a palpable upper abdominal mass and a cystic lesion is visualized on computed tomography scanning (see image below, asterisk marks the lesion).

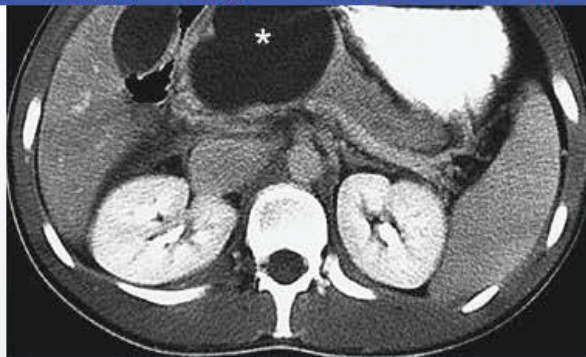


The inner walls of the lesion are most likely lined with:

- ☐ A. Glycogen-rich cuboidal epithelium
- ☐ B. Columnar mucinous epithelium







The inner walls of the lesion are most likely lined with:

- ☐ A. Glycogen-rich cuboidal epithelium
- ☒ B. Columnar mucinous epithelium
- ☐ C. Atypical cells forming papillary projections
- ☐ D. Fibrous and granulation tissue
- ☐ E. Endothelial cells





The inner walls of the lesion are most likely lined with:

- ☐ A. Glycogen-rich cuboidal epithelium (13%)
- ☐ B. Columnar mucinous epithelium (31%)
- ☐ C. Atypical cells forming papillary projections (5%)
- ☒ D. Fibrous and granulation tissue (42%)
- ☐ E. Endothelial cells (7%)

Correct

42%



01 min, 45 secs



12/23/2020

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End Block



This CT image shows a pancreatic pseudocyst, a potential complication of pancreatitis. In acute pancreatitis, proteolytic enzymes may disrupt the walls of the pancreatic ducts and cause leakage of pancreatic secretions into the peripancreatic space. This fluid has a high pancreatic enzyme content and induces an inflammatory reaction in the walls of the surrounding organs. Granulation tissue forms, encapsulating the fluid collection and forming a pseudocyst.

In contrast to a true cyst with walls lined by epithelial cells, the walls of a pseudocyst consist of granulation tissue and no epithelial lining. Fibrosis, thickening and organization of the walls occur with time. The formation of firm fibrotic pseudocyst walls ("maturation" of the pseudocyst) takes about 4 to 6 weeks following the episode of acute pancreatitis.

The most common location for a pseudocyst is in the lesser peritoneal sac, bordered by the stomach, duodenum and transverse colon. The pseudocyst walls are closely adherent to the surrounding hollow organs. The pseudocyst in the CT image above is located in the lesser sac, posterior to the stomach.

**(Choice A)** Glycogen-rich cuboidal epithelium is seen in serous pancreatic neoplasms.

**(Choice B)** Columnar mucinous epithelium is typically found in mucinous cystic neoplasms of the pancreas.







organs. The pseudocyst in the CT image above is located in the lesser sac, posterior to the stomach.

**(Choice A)** Glycogen-rich cuboidal epithelium is seen in serous pancreatic neoplasms.

**(Choice B)** Columnar mucinous epithelium is typically found in mucinous cystic neoplasms of the pancreas.

**(Choice C)** Atypical cells forming papillary projections are seen in the papillary variant of pancreatic adenocarcinoma.

**(Choice E)** Endothelial cells are not found in the wall of the pseudocyst.

### Educational Objective:

Pancreatic pseudocyst is a common complication of acute pancreatitis. It is a collection of fluid rich in enzymes and inflammatory debris. Its walls consist of granulation tissue and fibrosis. Unlike true cysts, pseudocysts are not lined by epithelium.

Pathology

Gastrointestinal & Nutrition

Acute pancreatitis

Subject

System

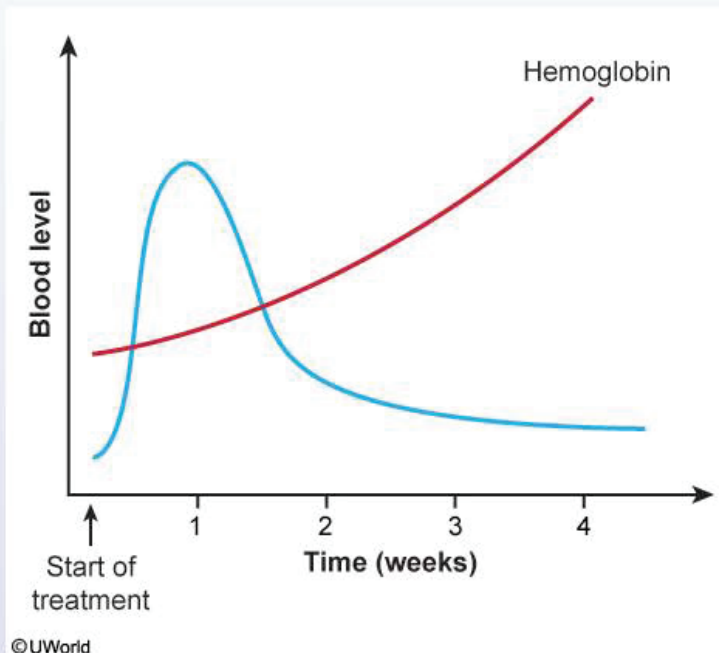
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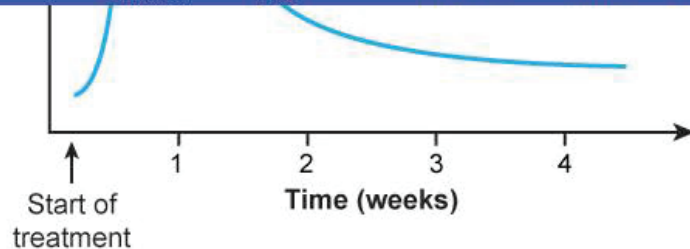


A 55-year-old man undergoing evaluation for fatigue and exertional dyspnea is diagnosed with macrocytic anemia. Upper gastrointestinal endoscopy is consistent with atrophic gastritis. He is started on intramuscular cyanocobalamin, with the resulting changes shown in the graph below.



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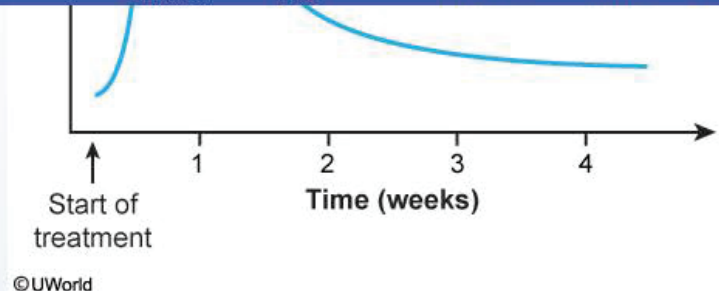
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The blue curve most likely corresponds to which of the following parameters?

- ☐ A. Erythrocyte count
- ☐ B. Gastrin
- ☐ C. Haptoglobin
- ☐ D. Methylmalonic acid
- ☐ E. Reticulocyte count

**Submit**





The blue curve most likely corresponds to which of the following parameters?

- ☒ A. Erythrocyte count (5%)
- ☐ B. Gastrin (2%)
- ☐ C. Haptoglobin (5%)
- ☐ D. Methylmalonic acid (25%)
- ☒ E. Reticulocyte count (60%)

Incorrect

Correct answer



60%



35 secs

Time spent



02/01/2021

Last updated

Block Time Remaining: 00:07:25

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End Block



The graph shows the treatment response to vitamin B<sub>12</sub> (cyanocobalamin) in a patient with **vitamin B<sub>12</sub> deficiency** secondary to atrophic gastritis. Vitamin B<sub>12</sub> deficiency impairs nucleic acid metabolism, causing delayed nuclear maturation and reduced cell division of erythrocyte precursors in the bone marrow (**megaloblastic anemia**).

Once vitamin B<sub>12</sub> **replacement therapy** is begun, erythrocyte precursors begin to change from megaloblastic to normoblastic. As the rate of effective erythropoiesis increases, immature erythrocytes (**reticulocytes**) are released from the bone marrow into the bloodstream. The peripheral count of these reticulocytes begins rising within 3 to 4 days and **peaks at around 1 week**, as indicated by the blue curve. The reticulocyte response peaks early during vitamin replacement as the reticulocytes that are initially released are left-shifted and take longer to mature in the circulation than later reticulocytes. However, hemoglobin levels (~1 g/week) are slower to rise, and the anemia typically takes as long as 8 weeks to correct.

**(Choice A)** The erythrocyte count curve would be expected to follow the contour of the hemoglobin curve as the total red blood cell pool returns to normal levels.

**(Choice B)** In chronic atrophic gastritis, parietal cell loss results in profound hypochlorhydria, increased serum gastrin levels, and inadequate intrinsic factor production. This patient most likely has elevated





as the total red blood cell pool returns to normal levels.

**(Choice B)** In chronic atrophic gastritis, parietal cell loss results in profound hypochlorhydria, increased serum gastrin levels, and inadequate intrinsic factor production. This patient most likely has elevated gastrin levels that would be unaffected by vitamin B<sub>12</sub> replacement.

**(Choice C)** Vitamin B<sub>12</sub> deficiency causes increased red cell breakdown due to ineffective erythropoiesis, and the resulting release of free hemoglobin leads to a decrease in serum haptoglobin levels. Haptoglobin levels would normalize (increase) with therapy.

**(Choice D)** Homocysteine and methylmalonic acid levels are elevated in vitamin B<sub>12</sub> deficiency due to decreased metabolism. In contrast, only homocysteine is elevated in folate deficiency. Vitamin B<sub>12</sub> replacement would cause a reduction in homocysteine and methylmalonic acid levels. However, the blue curve shows a high initial peak before declining, which is more consistent with the reticulocyte response.

### Educational objective:

Atrophic gastritis can result in profound hypochlorhydria, inadequate intrinsic factor production, vitamin B<sub>12</sub> deficiency, and elevated methylmalonic acid levels. The reticulocyte count increases dramatically once vitamin B<sub>12</sub> replacement therapy is initiated in an individual with pernicious anemia. Hemoglobin and erythrocyte count levels rise more gradually and take up to 8 weeks to normalize.







A 45-year-old man with a history of alcohol abuse, chronic hepatitis C, and HIV is brought to the emergency department due to altered mental status and abdominal distension. He is disoriented and unable to provide an adequate history. He is accompanied by a friend who reports the patient's heavy drinking habits. The patient's breath has a sweet, feculent odor. Physical examination shows gynecomastia, palmar erythema, and multiple spider angiomas. The abdomen is severely distended and dilated periumbilical veins are noted. There is 3+ bilateral lower extremity edema. Genital examination shows testicular atrophy. Neurologic examination shows disorientation and asterix. Abdominal imaging reveals splenomegaly. Which of the following findings in this patient has the same pathogenesis as his gynecomastia?

- ☐ A. Altered mental status
- ☐ B. Dilated periumbilical veins
- ☐ C. Lower extremity edema
- ☐ D. Spider angiomas
- ☐ E. Splenomegaly





emergency department due to altered mental status and abdominal distension. He is disoriented and unable to provide an adequate history. He is accompanied by a friend who reports the patient's heavy drinking habits. The patient's breath has a sweet, feculent odor. Physical examination shows gynecomastia, palmar erythema, and multiple spider angiomas. The abdomen is severely distended and dilated periumbilical veins are noted. There is 3+ bilateral lower extremity edema. Genital examination shows testicular atrophy. Neurologic examination shows disorientation and asterix. Abdominal imaging reveals splenomegaly. Which of the following findings in this patient has the same pathogenesis as his gynecomastia?

- ☐ A. Altered mental status
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- ☐ D. Spider angiomas
- ☐ E. Splenomegaly
- ☐ F. Sweet, feculent breath odor





drinking habits. The patient's breath has a sweet, feculent odor. Physical examination shows gynecomastia, palmar erythema, and multiple spider angiomas. The abdomen is severely distended and dilated periumbilical veins are noted. There is 3+ bilateral lower extremity edema. Genital examination shows testicular atrophy. Neurologic examination shows disorientation and asterix. Abdominal imaging reveals splenomegaly. Which of the following findings in this patient has the same pathogenesis as his gynecomastia?

- ☐ A. Altered mental status (8%)
- ☐ B. Dilated periumbilical veins (3%)
- ☐ C. Lower extremity edema (7%)
- ☒ D. Spider angiomas (70%)
- ☐ E. Splenomegaly (2%)
- ☐ F. Sweet, feculent breath odor (6%)

Correct

70%  
Answered correctly01 min, 10 secs  
Time Spent02/15/2021  
Last Updated

Block Time Remaining: 00:08:35

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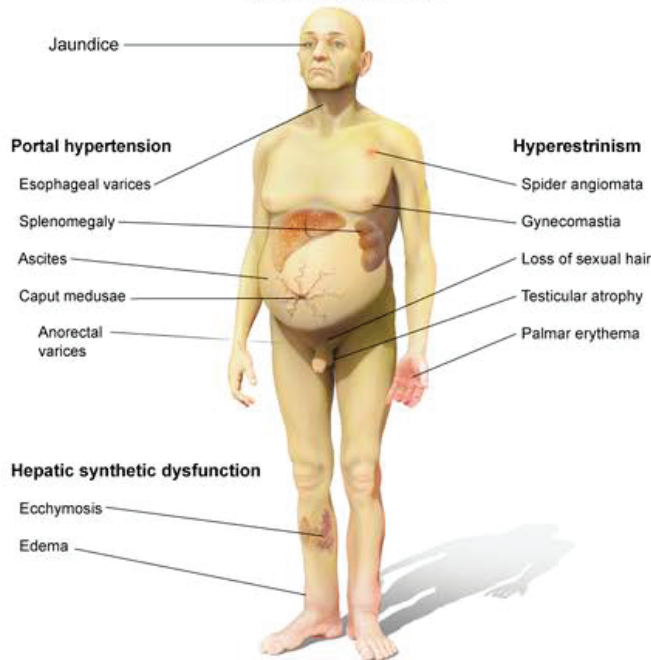
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## Exhibit Display

## Signs of liver cirrhosis



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This patient's numerous clinical findings are consistent with **liver cirrhosis**. In the cirrhotic patient, **gynecomastia** arises from **hyperestrinism** likely due to increased adrenal production of androstenedione with aromatization to estrone and eventual conversion to estradiol. Estradiol induces sex hormone-binding globulin production (primarily in the liver, but also in the uterus and testes), which results in increased testosterone binding and a decreased free testosterone/estrogen ratio. Impaired estrogen metabolism by the liver may also be a contributing factor. Other manifestations of hyperestrinism in the cirrhotic patient include spider angiomas and, in males, **testicular atrophy** with **decreased body hair**.

**Spider angiomas** are subcutaneous vascular lesions consisting of a central arteriole surrounded by many smaller vessels that blanch on compression. They are most frequently found on the trunk, face, and upper limbs. Acquired spider angiomas may also occur with other hyperestrogenic states (eg, pregnancy), possibly due to estrogen's effects on arteriolar dilation. The number and size of these skin lesions generally correlate with the severity of liver disease.

**(Choices A and F)** Altered mental status and malodorous, sweet, feculent breath (feto hepaticus) are signs of poor hepatic function and accumulation of metabolic toxins (eg, ammonia, dimethyl sulfide). In the healthy liver, ammonia is detoxified to urea, which is then excreted in the urine. In the cirrhotic liver,





Item 10 of 40

Question Id: 100



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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### Exhibit Display

#### Spider angioma



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possibly due to estrogen's effects on arteriolar dilation. The number and size of these skin lesions generally correlate with the severity of liver disease.

**(Choices A and F)** Altered mental status and malodorous, sweet, feculent breath (feto hepaticus) are signs of poor hepatic function and accumulation of metabolic toxins (eg, ammonia, dimethyl sulfide). In the healthy liver, ammonia is detoxified to urea, which is then excreted in the urine. In the cirrhotic liver, ammonia accumulates in the blood, resulting in impaired neurotransmission in the central nervous system and possible brain edema.

**(Choices B and E)** Portal hypertension arises from increased hepatic resistance to portal flow at the sinusoids. This causes increased hydrostatic pressure at the portosystemic collateral veins in the anterior abdomen (eg, caput medusae), lower rectum (eg, anorectal varices), and lower esophagus (eg, esophageal varices). Portal hypertension also leads to ascites and venous congestion of the spleen (eg, splenomegaly).

**(Choice C)** The liver is the primary site of protein synthesis. Liver cirrhosis can result in decreased albumin production, leading to lower intravascular oncotic pressure with fluid extravasation and pitting edema in the lower extremities (pedal edema).

### Educational objective:

Hyperestrinism in liver cirrhosis likely arises due to increases in androstenedione production androgen



and possible brain edema.

**(Choices B and E)** Portal hypertension arises from increased hepatic resistance to portal flow at the sinusoids. This causes increased hydrostatic pressure at the portosystemic collateral veins in the anterior abdomen (eg, caput medusae), lower rectum (eg, anorectal varices), and lower esophagus (eg, esophageal varices). Portal hypertension also leads to ascites and venous congestion of the spleen (eg, splenomegaly).

**(Choice C)** The liver is the primary site of protein synthesis. Liver cirrhosis can result in decreased albumin production, leading to lower intravascular oncotic pressure with fluid extravasation and pitting edema in the lower extremities (pedal edema).

### Educational objective:

Hyperestrogenism in liver cirrhosis likely arises due to increases in androstenedione production, androgen aromatization, and sex hormone-binding globulin concentration (preferentially binds testosterone). Impaired estrogen metabolism by the liver may also be a contributing factor. A decreased free testosterone/estrogen ratio leads to gynecomastia, testicular atrophy, decreased body hair, and spider angiomas.

### References



A 34-year-old man is found to have dyslipidemia. His other medical problems include a myocardial infarction 1 week ago. His father died of myocardial infarction at the age of 48 years. Several other family members have had myocardial infarctions and hypertension. The patient smoked cigarettes and drank alcohol occasionally but quit after his myocardial infarction. He is started on simvastatin and cholestyramine. Which of the following best describes the independent effects of simvastatin and cholestyramine, respectively, on hepatic cholesterol synthesis?

- ☐ A. Increase and increase
- ☐ B. Increase and decrease
- ☐ C. Decrease and increase
- ☐ D. Decrease and decrease
- ☐ E. Increase and no change

**Submit**





A 34-year-old man is found to have dyslipidemia. His other medical problems include a myocardial infarction 1 week ago. His father died of myocardial infarction at the age of 48 years. Several other family members have had myocardial infarctions and hypertension. The patient smoked cigarettes and drank alcohol occasionally but quit after his myocardial infarction. He is started on simvastatin and cholestyramine. Which of the following best describes the independent effects of simvastatin and cholestyramine, respectively, on hepatic cholesterol synthesis?

- ☐ A. Increase and increase (2%)
- ☐ B. Increase and decrease (2%)
- ☒ C. Decrease and increase (72%)
- ☐ D. Decrease and decrease (19%)
- ☐ E. Increase and no change (3%)

Correct



72%

Answered correctly



56 secs

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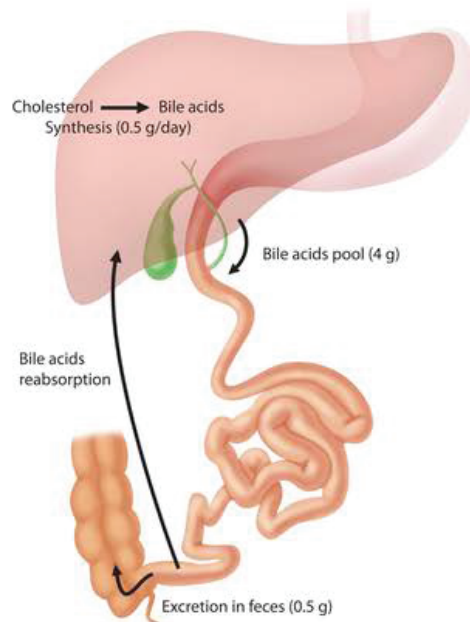


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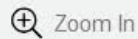


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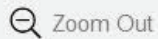
## Bile acid metabolism



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Bile acids are synthesized in the liver from cholesterol catabolism. Bile enters the duodenum through gallbladder contraction. Bile acids are primarily absorbed in the terminal ileum, with the small amount that remains unabsorbed being excreted in the stool (this amount is matched by bile acid synthesis).

**Statins** are the first-line therapy for most patients with hypercholesterolemia. These drugs competitively **inhibit HMG CoA reductase**, the enzyme responsible for the conversion of HMG CoA to mevalonate (ie, the rate-limiting step in hepatic cholesterol synthesis). This inhibition **decreases hepatic cholesterol synthesis**. The resulting upregulation of LDL receptors causes increased uptake of LDL from the circulation. Statins are very effective in reducing LDL cholesterol. Statins' effects on triglyceride and HDL levels are comparatively modest.

**Bile acid-binding resins** (ie, bile acid sequestrants) work by binding bile acids in the gastrointestinal tract, thereby interfering with the enterohepatic circulation of bile acids and causing increased bile acid excretion. This results in hepatic **synthesis of new bile acids**, a process that consumes liver cholesterol stores. Hepatic uptake of LDL from the circulation is increased for continued bile acid synthesis. Bile acid production and secretion are increased by 10-fold due to this interruption of the enterohepatic circulation of bile acids. Hepatic cholesterol reduction is an activating factor for HMG CoA reductase and subsequently







excretion. This results in hepatic **synthesis of new bile acids**, a process that consumes liver cholesterol stores. Hepatic uptake of LDL from the circulation is increased for continued bile acid synthesis. Bile acid production and secretion are increased by 10-fold due to this interruption of the enterohepatic circulation of bile acids. Hepatic cholesterol reduction is an activating factor for HMG CoA reductase and subsequently results in **increased hepatic cholesterol synthesis**. This effect can be blocked with the addition of a statin drug to the treatment regimen, leading to a greater reduction in LDL levels than with use of either drug alone (synergistic action).

### Educational objective:

Simvastatin decreases hepatic cholesterol production, while cholestyramine increases hepatic cholesterol and bile acid synthesis. Combination therapy results in a synergistic reduction in plasma LDL level.

### References

- [Overview of pharmacologic therapy for the treatment of dyslipidemia.](#)

Pharmacology

Gastrointestinal &amp; Nutrition

Dyslipidemia

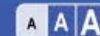
Subject

System

Topic

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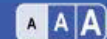




A 1-month-old, full-term African-American boy is brought to the office for a routine check-up. He is exclusively breastfed. The boy does not have any medical problems, and his hospital stay after birth was unremarkable. His mother consumes a well-balanced diet, takes no medications, and does not drink alcohol. The boy is at the 50th percentile for weight and the 60th percentile for height. His physical examination is normal. At this time, supplementation with which of the following should be recommended for this infant?

- ☐ A. Folic acid
- ☐ B. Iron
- ☐ C. Riboflavin
- ☐ D. Thiamine
- ☐ E. Vitamin A
- ☐ F. Vitamin D

**Submit**



A 1-month-old, full-term African-American boy is brought to the office for a routine check-up. He is exclusively breastfed. The boy does not have any medical problems, and his hospital stay after birth was unremarkable. His mother consumes a well-balanced diet, takes no medications, and does not drink alcohol. The boy is at the 50th percentile for weight and the 60th percentile for height. His physical examination is normal. At this time, supplementation with which of the following should be recommended for this infant?

- ☐ A. Folic acid (4%)
- ☐ B. Iron (15%)
- ☐ C. Riboflavin (2%)
- ☐ D. Thiamine (3%)
- ☐ E. Vitamin A (5%)
- ☒ F. Vitamin D (68%)







Supplementation for breastfed infants	
Supplement	Risk factors
Vitamin D	<ul style="list-style-type: none"><li>• Exclusive breastfeeding</li><li>• Lack of sunlight exposure</li><li>• Dark skin pigmentation</li></ul>
Iron	<ul style="list-style-type: none"><li>• Preterm/low-birthweight</li></ul>

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**Breast milk** is the gold standard of infant nutrition; it contains proteins, carbohydrates, fats, vitamins, trace minerals, immunoglobulins, amino acids, and enzymes. All vitamins and trace minerals are present in adequate amounts **except vitamins D and K**. Vitamin K is supplemented by an intramuscular injection at delivery to prevent hemorrhagic disease in the newborn.

Regular **sunlight** exposure typically provides sufficient vitamin D. However, infants are generally shielded from direct sunlight due to sunburn risk. In addition, infants with dark skin pigmentation require more sunlight exposure to produce adequate vitamin D. Melanin is a natural sunblock and prevents ultraviolet





Regular **sunlight** exposure typically provides sufficient vitamin D. However, infants are generally shielded from direct sunlight due to sunburn risk. In addition, infants with dark skin pigmentation require more sunlight exposure to produce adequate vitamin D. Melanin is a natural sunblock and prevents ultraviolet rays from reaching the skin for **vitamin D synthesis**. Prolonged vitamin D insufficiency can lead to rickets (inadequate bone and cartilage mineralization). Therefore, all **exclusively breastfed** infants should receive **vitamin D supplementation to prevent rickets**. Formula-fed infants do not require supplementation as formula is fortified with adequate amounts of vitamin D.

**(Choices A, C, and D)** Human breast milk normally provides adequate amounts of folic acid, riboflavin, and thiamine for full-term infants.

**(Choice B)** Although breast milk has low iron content, the bioavailability of iron in breastmilk is considerably higher than supplemental iron and is sufficient for infants until age 4 months. Due to decreasing iron concentration in breast milk over time, supplementation is recommended for breastfed infants at age >4 months until solid food intake provides an adequate amount.

**(Choice E)** Vitamin A stores in the liver are low at birth but rapidly increase due to the large amount in colostrum and breast milk.

**Educational objective:**





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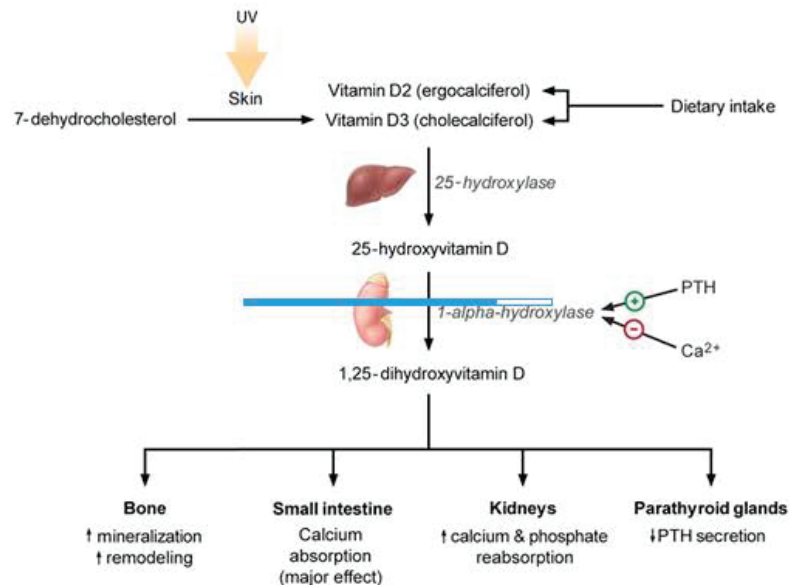
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Regular sunlight exposure typically provides sufficient vitamin D. However, infants are generally shielded

### Exhibit Display

#### Normal vitamin D metabolism



PTH = parathyroid hormone.  
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supplementation as formula is fortified with adequate amounts of vitamin D.

**(Choices A, C, and D)** Human breast milk normally provides adequate amounts of folic acid, riboflavin, and thiamine for full-term infants.

**(Choice B)** Although breast milk has low iron content, the bioavailability of iron in breastmilk is considerably higher than supplemental iron and is sufficient for infants until age 4 months. Due to decreasing iron concentration in breast milk over time, supplementation is recommended for breastfed infants at age >4 months until solid food intake provides an adequate amount.

**(Choice E)** Vitamin A stores in the liver are low at birth but rapidly increase due to the large amount in colostrum and breast milk.

### Educational objective:

The breast milk content of vitamins D and K is typically insufficient for the nutritional needs of the newborn. Vitamin K is given parenterally to all newborns at birth to prevent hemorrhagic disease of the newborn. Exclusively breastfed infants require vitamin D supplementation due to lack of sunlight exposure and to prevent rickets.

### References

- Is vitamin D supplementation necessary in healthy full-term breastfed infants? A follow-up study of bone





A 4-week-old boy is brought to the office for a routine well-baby visit. The boy has been exclusively breastfeeding every 2-3 hours and is making 6 or 7 wet diapers a day. His urine has appeared dark yellow, and he has had a few pale-colored stools. His parents also noticed that his skin has appeared yellow for the past 2 weeks, but they were not concerned as they heard from friends that yellow skin is common with breastfeeding. The patient was born full term without complications by vaginal delivery to a primigravida. On physical examination, he is well-appearing with icteric sclerae and jaundice of the head and upper chest. Abdominal examination reveals a mildly enlarged and firm liver. Liver function results are as follows:

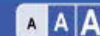
Total bilirubin 7.3 mg/dL

Direct bilirubin 5 mg/dL

Which of the following is the most likely mechanism for the patient's presentation?

- ☐ A. Extrahepatic obstruction of bile ducts
- ☐ B. Genetic mutation causing reduced glucuronidation
- ☐ C. Impaired galactose metabolism





On physical examination, he is well-appearing with icteric sclerae and jaundice of the head and upper chest. Abdominal examination reveals a mildly enlarged and firm liver. Liver function results are as follows:

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- ☐ A. Extrahepatic obstruction of bile ducts
- ☐ B. Genetic mutation causing reduced glucuronidation
- ☐ C. Impaired galactose metabolism
- ☐ D. Increased enterohepatic circulation of bilirubin
- ☐ E. Maternal antibody-mediated red blood cell destruction

Submit





On physical examination, he is well-appearing with **icteric sclerae** and jaundice of the head and upper chest. Abdominal examination reveals a mildly enlarged and firm liver. Liver function results are as follows:

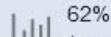
Total bilirubin 7.3 mg/dL

Direct bilirubin 5 mg/dL

Which of the following is the most likely mechanism for the patient's presentation?

- ☒ A. Extrahepatic obstruction of bile ducts (62%)
- ☐ B. Genetic mutation causing reduced glucuronidation (20%)
- ☐ C. Impaired galactose metabolism (3%)
- ☐ D. Increased enterohepatic circulation of bilirubin (9%)
- ☐ E. Maternal antibody-mediated red blood cell destruction (3%)

Correct



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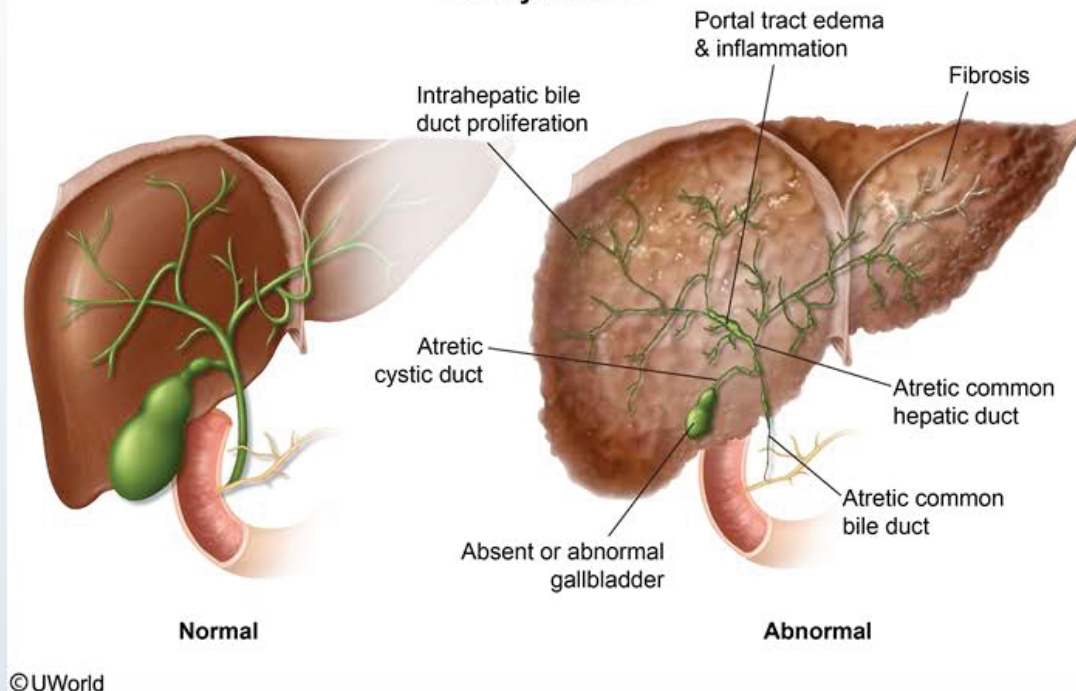
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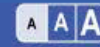


## Biliary atresia



**Biliary atresia** is a progressive, complete or partial **obstruction** of **extrahepatic bile ducts**. The biliary





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**Biliary atresia** is a progressive, complete or partial **obstruction** of **extrahepatic bile ducts**. The biliary tree is normal at birth and subsequently undergoes destruction that is thought to be immune-related or viral-induced. Infants may appear healthy at birth, but then present with **jaundice** within the first 2 months of life, along with **dark urine** and **acholic** (pale or clay-colored) **stools** due to excessive renal excretion of bilirubin and lack of intestinal bile, respectively. Physical examination may also reveal firm hepatomegaly due to inflammation. Laboratory findings, including **elevated direct bilirubin** and gamma-glutamyl transferase, are consistent with cholestasis.

Liver biopsy is usually diagnostic and reveals intrahepatic bile duct proliferation, portal tract edema, and fibrosis. Urgent surgical intervention is required, as lack of intervention can lead to death (due to cirrhosis) usually within 2 years.

**(Choice B)** Gilbert syndrome is an inherited, benign condition of reduced production of glucuronyl transferase, a hepatic enzyme responsible for **glucuronidation** (ie, conversion of bilirubin to its excretable form). Patients are usually asymptomatic except at times of stress (eg, fasting, illness) during which mild, indirect hyperbilirubinemia and jaundice are present.

**(Choice C)** Galactosemia (galactose-1-phosphate uridyl transferase [GALT] deficiency) is characterized by

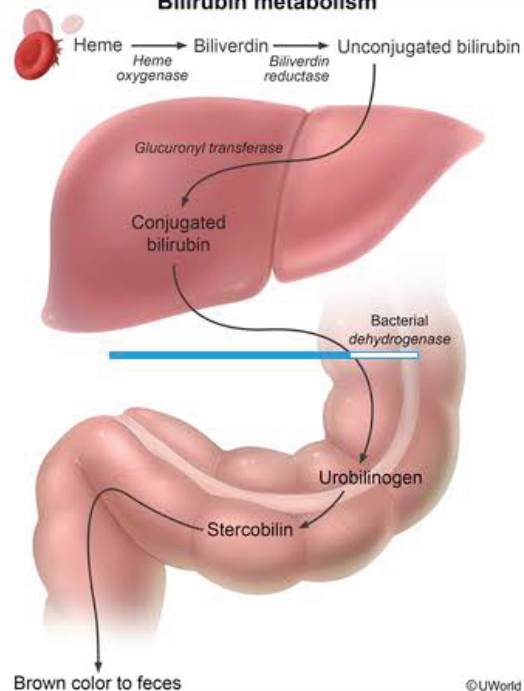






## Exhibit Display

## Bilirubin metabolism



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form). Patients are usually asymptomatic except at times of stress (eg, fasting, illness) during which mild, indirect hyperbilirubinemia and jaundice are present.

**(Choice C)** Galactosemia (galactose-1-phosphate uridyl transferase [GALT] deficiency) is characterized by defective metabolism of galactose, a breakdown product of lactose that is then normally metabolized to glucose. Both direct and indirect bilirubin levels may be elevated. However, infants would present with vomiting, diarrhea, and lethargy during the first few days of life due to inability to digest breast milk or formula.

**(Choice D)** Breast milk jaundice causes an indirect hyperbilirubinemia that peaks at age 2 weeks. The pathogenesis likely involves an enzyme, beta-glucuronidase, in breast milk that deconjugates bilirubin. This causes increased absorption and, therefore, increased enterohepatic circulation of bilirubin. Urine and stool appearance are unaffected.

**(Choice E)** Hemolytic disease of the newborn can result from Rh incompatibility (eg, Rh-positive infant and Rh-negative mother) or ABO incompatibility (eg, A+ infant and O+ mother). Patients develop jaundice on the first day of life due to indirect hyperbilirubinemia, and a positive direct Coombs (antiglobulin) test confirms the presence of antibody-mediated hemolysis.

**Educational objective:**

Differential diagnosis of neonatal hyperbilirubinemia: neonatal jaundice, neonatal hemolysis, neonatal liver disease



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### Educational objective:

Biliary atresia, or obstruction of extrahepatic bile ducts, presents with jaundice, dark urine, and acholic stools in the first 2 months of life due to conjugated hyperbilirubinemia. Biopsy reveals intrahepatic bile duct proliferation, portal tract edema, and fibrosis.

### References

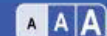




A 36-year-old woman comes to the office due to vague epigastric abdominal pain, occasional nausea, and bloating. She has no associated weight loss. Medical history is notable for moderate obesity and chronic allergic rhinitis. The patient takes no medications and does not use tobacco, alcohol, or illicit drugs. She was a vegetarian for several years but now consumes a wide variety of foods, including meat products. The patient has traveled abroad extensively in the past. Vital signs are normal. Examination shows mild epigastric tenderness to deep palpation. Laboratory results reveal mild anemia. Upper gastrointestinal endoscopy shows diffuse erythema of the antral mucosa. Biopsy reveals an inflammatory cell infiltrate involving the superficial mucosal layers. The underlying cause of this patient's current condition can also lead to which of the following?

- ☐ A. Gastric lymphoma
- ☐ B. Gastroparesis
- ☐ C. Gluten intolerance
- ☐ D. Ileal obstruction
- ☐ E. Pernicious anemia





allergic rhinitis. The patient takes no medications and does not use tobacco, alcohol, or illicit drugs. She was a vegetarian for several years but now consumes a wide variety of foods, including meat products. The patient has traveled abroad extensively in the past. Vital signs are normal. Examination shows mild epigastric tenderness to deep palpation. Laboratory results reveal mild anemia. Upper gastrointestinal endoscopy shows diffuse erythema of the antral mucosa. Biopsy reveals an inflammatory cell infiltrate involving the superficial mucosal layers. The underlying cause of this patient's current condition can also lead to which of the following?

- ☒ A. Gastric lymphoma (55%)
- ☐ B. Gastroparesis (2%)
- ☐ C. Gluten intolerance (6%)
- ☐ D. Ileal obstruction (1%)
- ☐ E. Pernicious anemia (33%)

Correct

55%



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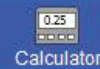
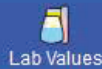
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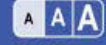
### Atrophic gastritis

	<i>Helicobacter pylori</i> -induced chronic gastritis	Autoimmune gastritis
<b>Distribution</b>	Multifocal; patchy	Corpus; diffuse (spares antrum)
<b>Inflammatory cells</b>	Neutrophils, plasma cells, lymphocytes	Lymphocytes, macrophages
<b>Gastrin level</b>	Normal or ↓	↑
<b>Acid production</b>	Normal or ↓	↓
<b>Sequelae</b>	Gastric ulcer*	Vitamin B <sub>12</sub> deficiency/pernicious anemia
<b>Associated malignancy</b>	Adenocarcinoma, MALT lymphoma	Adenocarcinoma, carcinoid
<b>Risk factors</b>	Poverty, living in developing country	Other autoimmune diseases

**MALT** = mucosa-associated lymphoid tissue.







**MALT** – mucosa-associated lymphoid tissue.

\*Chronic *H pylori* infection is more associated with gastric ulcers; acute infection is more associated with duodenal ulcers

This patient with **antral-predominant** gastritis likely has an **acute** *Helicobacter pylori* infection, which typically presents as nonatrophic gastritis. Destruction of somatostatin-producing cells in the antrum leads to **unchecked gastrin secretion** and results in excess production of stomach acid and an increased risk of **duodenal ulcers**.

If left untreated, **chronic** *H pylori* infection typically **spreads** to involve the corpus (body) and fundus of the stomach and is characterized by patchy, **multifocal gastric atrophy** with intestinal metaplasia. Patchy destruction of parietal and G cells results in **diminished acid secretion** and hypochlorhydria. Patients with chronic gastritis are less likely to develop duodenal ulcers but due to the associated **chronic inflammation**, they are at increased risk of **gastric ulcers** and malignancy, particularly **gastric lymphoma** (ie, mucosa-associated lymphoid tissue [MALT] lymphoma) and gastric adenocarcinoma.

**(Choice B)** *H pylori*–associated ulcers can cause gastric outlet obstruction, not gastroparesis, which is commonly due to uncontrolled diabetes or infiltrative diseases (eg, scleroderma).

**(Choice C)** Celiac disease is an immune-mediated response to a protein in gluten and can cause





Item 14 of 40

Question Id: 1918



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



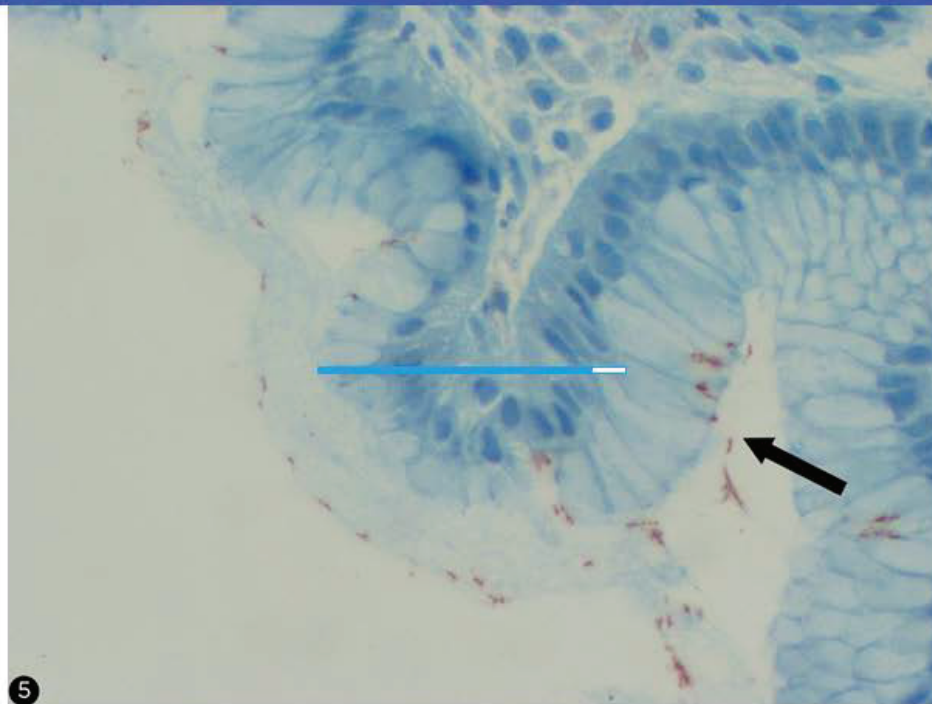
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MACT - mucosa-associated lymphoid tissue.

Exhibit Display



5

Zoom In

Zoom Out

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Block Time Remaining: 00:14:44

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1



Feedback



Suspend



End Block



commonly due to uncontrolled diabetes or infiltrative diseases (eg, scleroderma).

**(Choice C)** Celiac disease is an immune-mediated response to a protein in gluten and can cause microcytic anemia due to iron malabsorption. Autoimmune diseases are associated with autoimmune gastritis, not *H pylori* infection.

**(Choice D)** Ileal obstruction can occur due to Crohn disease, which can also cause abdominal pain and blood-loss anemia. However, *H pylori* infects gastric mucosa; the ileum is typically unaffected.

**(Choice E)** Unlike chronic *H pylori*-associated atrophic gastritis, which causes patchy atrophy with sparing of some parietal cells (allowing for continued intrinsic factor production and B<sub>12</sub> absorption), autoimmune gastritis is characterized by diffuse and more complete immune-mediated destruction of parietal cells and intrinsic factor. This results in impaired vitamin B<sub>12</sub> absorption and pernicious anemia.

### Educational objective:

Acute *Helicobacter pylori* infection initially causes nonatrophic antral gastritis and an increased risk for duodenal ulcers. Chronic infection results in patchy, multifocal, atrophic gastritis with loss of parietal cells and G cells in the gastric body; this is associated with decreased acid secretion and an increased risk of gastric ulcers, gastric adenocarcinoma, and MALT lymphoma.







A 65-year-old woman comes to the emergency department due to nausea, vomiting, and abdominal pain that began about 6 hours ago. She has also had vague pelvic pain over the last few months but says her pain has never been this severe. Temperature is 38.4 C (101 F), blood pressure is 141/90 mm Hg, pulse is 92/min, and respirations are 18/min. Physical examination shows a moderately distended abdomen. There is a tender bulge below the inguinal ligament, lateral to the pubic tubercle. The overlying skin is erythematous. Which of the following structures is most likely immediately lateral to the bulge?

- ☐ A. Femoral vein
- ☐ B. Inferior epigastric vessels
- ☐ C. Pectineal ligament
- ☐ D. Rectus muscle sheath
- ☐ E. Round ligament
- ☐ F. Transversalis fascia

**Submit**

Block Time Remaining: 00:14:45

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A 65-year-old woman comes to the emergency department due to nausea, vomiting, and abdominal pain that began about 6 hours ago. She has also had vague pelvic pain over the last few months but says her pain has never been this severe. Temperature is 38.4 C (101 F), blood pressure is 141/90 mm Hg, pulse is 92/min, and respirations are 18/min. Physical examination shows a moderately distended abdomen. There is a tender bulge below the inguinal ligament, lateral to the pubic tubercle. The overlying skin is erythematous. Which of the following structures is most likely immediately lateral to the bulge?

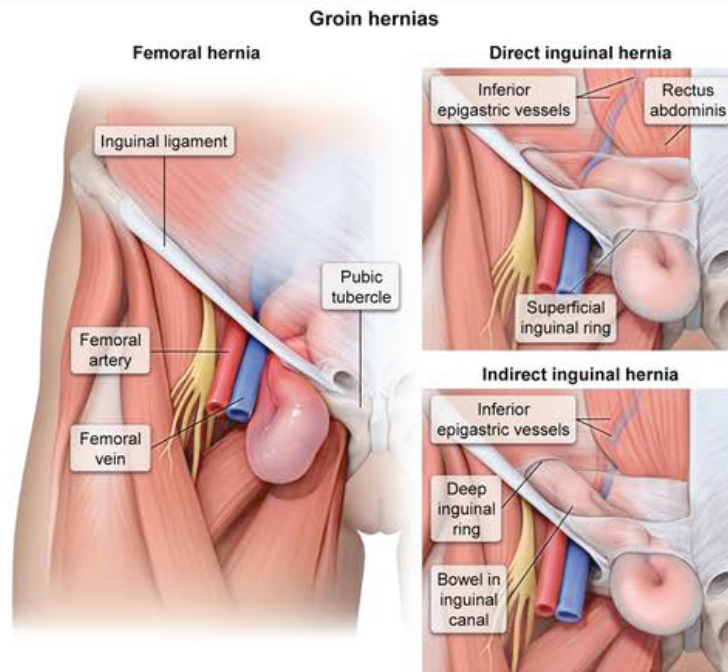
- ☒ A. Femoral vein (71%)
- ☐ B. Inferior epigastric vessels (17%)
- ☐ C. Pectineal ligament (2%)
- ☐ D. Rectus muscle sheath (2%)
- ☐ E. Round ligament (3%)
- ☐ F. Transversalis fascia (2%)



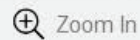


## Groin hernias

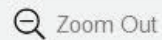
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This patient has a **femoral hernia**, which characteristically presents with upper thigh, groin, or pelvic discomfort and a tender bulge **below the inguinal ligament**, lateral to the pubic tubercle and lacunar ligament. Femoral hernias are more common in women and tend to occur on the right side. Advanced age is the most important risk factor. Over time, the femoral ring becomes lax and can widen, allowing bowel to protrude into the femoral canal, the medial most compartment within the femoral sheath. The femoral vessels travel within other compartments of the femoral sheath, with the **femoral vein** running **immediately lateral** to the hernia.

Because the femoral canal is small, femoral hernias are prone to **incarceration**. Incarcerated hernias cannot be reduced; if a segment of bowel is present in the hernia sac, incarceration can cause bowel obstruction (eg, nausea, vomiting, abdominal pain and distension). Incarceration can also cause impaired blood flow to contents trapped in the hernia sac, resulting in **strangulation** (ischemia and necrosis) with potential systemic complications such as sepsis.

**(Choice B)** Direct inguinal hernias protrude through weakened transversalis fascia, medial to the inferior epigastric vessels, and emerge into the Hesselbach triangle. Indirect inguinal hernias protrude lateral to the inferior epigastric vessels before running through the deep (internal) inguinal ring and into the inguinal canal.





**(Choice C)** The pectineal ligament (inguinal ligament of Cooper) is a thickened part of the pectineal fascia. It overlies the pectineal ridge of the pubic bone and is located posterior to the femoral canal.

**(Choice D)** The rectus muscle sheath forms the medial border of the **Hesselbach triangle**. Direct inguinal hernias are located just lateral to the rectus abdominis muscle sheath.

**(Choice E)** The round ligament in women is homologous to the spermatic cord in men. It leaves the pelvis through the deep inguinal ring and passes through the inguinal canal.

**(Choice F)** The transversalis fascia is found between the transversalis muscle and the extraperitoneal fat. It forms the posterior wall of the inguinal canal. The deep (internal) inguinal ring is an opening in the transversalis fascia and is the site of protrusion of indirect inguinal hernias.

### **Educational objective:**

Femoral hernias can present with groin discomfort and a tender bulge on the upper thigh inferior to the inguinal ligament, lateral to the pubic tubercle and lacunar ligament. The structure that lies immediately lateral to the hernia within the femoral sheath is the femoral vein. Incarceration and strangulation are common complications of femoral hernias.





Item 15 of 40

Question Id: 417



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



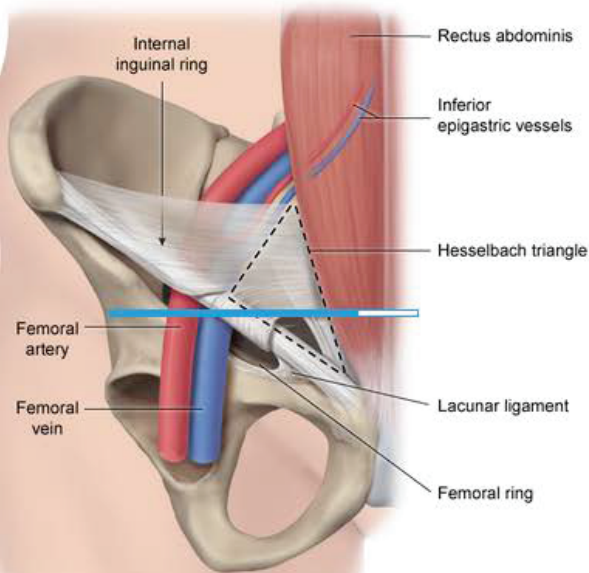
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## Exhibit Display

## Groin hernias



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Feedback



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End Block





A 46-year-old obese man is referred to a dietitian for evaluation of his food intake. He has been trying to lose weight but has been unsuccessful. The patient is 172.7 cm (5 ft 8 in) tall and weighs 113 kg (250 lb). Analysis of his food intake shows that he is consuming 3600 Calories a day. The dietitian recommends increasing physical activity and implementing a dietary plan. In the first phase, the patient is advised to reduce his daily dietary intake to 3,000 Calories, with 30% coming from protein. How much protein per day will this patient consume on the new dietary plan?

- ☐ A. 130 g
- ☐ B. 160 g
- ☐ C. 180 g
- ☐ D. 225 g
- ☐ E. 250 g

**Submit**



A 46-year-old obese man is referred to a dietitian for evaluation of his food intake. He has been trying to lose weight but has been unsuccessful. The patient is 172.7 cm (5 ft 8 in) tall and weighs 113 kg (250 lb). Analysis of his food intake shows that he is consuming 3600 Calories a day. The dietitian recommends increasing physical activity and implementing a dietary plan. In the first phase, the patient is advised to reduce his daily dietary intake to 3,000 Calories, with 30% coming from protein. How much protein per day will this patient consume on the new dietary plan?

- ☐ A. 130 g (8%)
- ☐ B. 160 g (6%)
- ☐ C. 180 g (17%)
- ☒ D. 225 g (58%)
- ☐ E. 250 g (8%)

Correct



58%

Answered correctly



01 min, 06 secs

Time Spent



09/13/2020

Last Updated

Block Time Remaining: 00:16:27

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Feedback



Suspend



End Block



### Explanation

Dietary energy comes predominantly from protein, carbohydrate, and fat. Metabolism yields 4 Calories (Cal) per gram of protein or carbohydrate and 9 Cal per gram of fat. Ethanol yields 7 Cal per gram.

This patient is instructed to consume 3000 Cal per day, 900 (30%) of which are to be from protein.

Because 1 g of protein yields 4 Cal of energy, this patient should consume  $(900 \text{ Cal} / 4 \text{ Cal}) = 225 \text{ g/day}$  of protein.

### Educational objective:

Metabolism of 1 g of protein or carbohydrate produces 4 Calories of energy; metabolism of 1 g of fat produces 9 Calories.

Biochemistry

Subject

Gastrointestinal & Nutrition

System

Obesity

Topic

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A 42-year-old man comes to the office with rectal bleeding. He used to have occasional streaks of blood on the tissue after wiping, but for the past several days he has seen blood dripping into the toilet at the end of defecation. The patient reports chronic constipation and has to strain while having a bowel movement but has no rectal or abdominal pain. He works as a truck driver, and his diet consists mainly of hamburgers and French fries. Abdominal examination is unremarkable. There is no mass or tenderness on digital rectal examination, but anoscopy shows bulging purplish-blue mucosal lesions above the dentate line. Rubber band ligation of the lesions is most likely to involve which of the following?

- ☐ A. Deep external pudendal artery branches
- ☐ B. External iliac vein tributaries
- ☐ C. Inferior mesenteric vein tributaries
- ☐ D. Internal pudendal vein tributaries
- ☐ E. Left colic artery branches
- ☐ F. Superior vesical artery branches





A 42-year-old man comes to the office with **rectal bleeding**. He used to have occasional streaks of blood on the tissue after wiping, but for the past several days he has seen blood dripping into the toilet at the end of defecation. The patient reports chronic constipation and has to strain while having a bowel movement but has no rectal or abdominal pain. He works as a truck driver, and his diet consists mainly of hamburgers and French fries. Abdominal examination is unremarkable. There is no mass or tenderness on digital rectal examination, but anoscopy shows bulging purplish-blue mucosal lesions above the dentate line. Rubber band ligation of the lesions is most likely to involve which of the following?

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- ☐ E. Left colic artery branches
- ☐ F. Superior vesical artery branches





on the tissue after wiping, but for the past several days he has seen blood dripping into the toilet at the end of defecation. The patient reports chronic constipation and has to strain while having a bowel movement but has no rectal or abdominal pain. He works as a truck driver, and his diet consists mainly of hamburgers and French fries. Abdominal examination is unremarkable. There is no mass or tenderness on digital rectal examination, but anoscopy shows bulging purplish-blue mucosal lesions above the dentate line. Rubber band ligation of the lesions is most likely to involve which of the following?

- ☐ A. Deep external pudendal artery branches (3%)
- ☐ B. External iliac vein tributaries (4%)
- ☒ C. Inferior mesenteric vein tributaries (62%)
- ☐ D. Internal pudendal vein tributaries (24%)
- ☐ E. Left colic artery branches (2%)
- ☐ F. Superior vesical artery branches (2%)

Correct



62%

Answered correctly



01 min, 17 secs

Time spent



01/20/2021

Last updated

Block Time Remaining: 00:17:44

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Feedback



Suspend



End Block





Item 17 of 40

Question Id: 11840



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



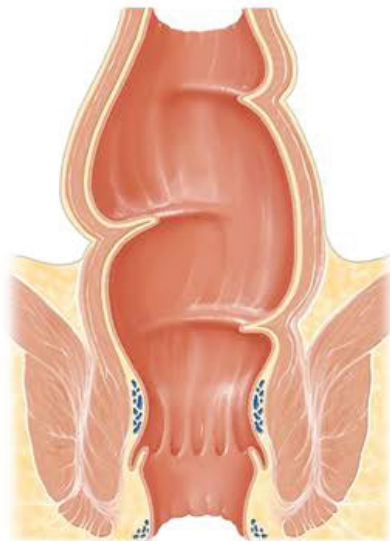
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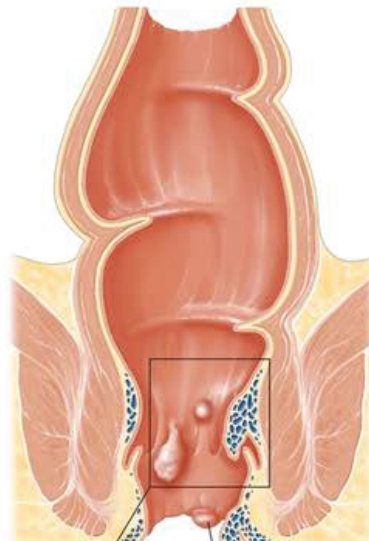
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### Exhibit Display

Normal venous plexus



Hemorrhoids



Internal hemorrhoids

External hemorrhoids

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Hemorrhoids are classified based on their relation to the dentate line in the anal canal, with **internal hemorrhoids** originating **above the line** and external hemorrhoids below. They result from abnormal distension of the anal **arteriovenous plexus**, which normally forms the anal cushions (composed of venous sinusoids and connective tissue) that are important for maintaining fecal continence. Chronically increased venous pressure due to prolonged straining or breakdown of supporting tissue due to advancing age can cause the cushions to bulge into the anal canal, where they can become inflamed, thrombose, or prolapse.

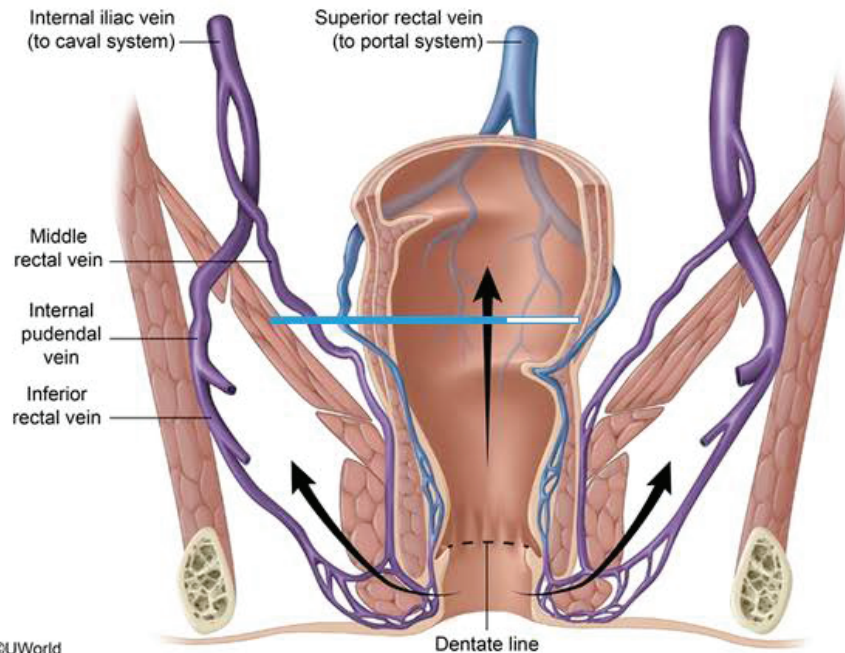
Hemorrhoids can be treated with rubber band ligation, which cuts off the blood supply to the lesions and causes them to degenerate. The venous components of internal hemorrhoids drain into the **superior rectal vein**, which communicates with the **inferior mesenteric vein**. External hemorrhoids drain via the inferior rectal vein into the internal pudendal vein, which communicates with the internal iliac veins (**Choice D**). Internal hemorrhoids have no somatic sensory innervation and cannot cause pain; however, external hemorrhoids are innervated by the same nerves that cover the perianal area and can be very sensitive to pain.

(**Choice A**) Branches of the deep external pudendal artery supply the scrotum (labia majora in females) and the perineum.



## Exhibit Display

## Anorectal venous drainage



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Dentate line

Zoom In

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**(Choice A)** Branches of the deep external pudendal artery supply the scrotum (labia majora in females) and the perineum.

**(Choice B)** The external iliac vein receives drainage from the inferior epigastric and deep circumflex iliac veins, which serve the anterior abdominal wall and iliac crest, respectively.

**(Choice E)** The left colic artery branches off the inferior mesenteric artery to supply the transverse and descending colon.

**(Choice F)** The superior vesical artery and its branches supply portions of the urinary bladder and ductus deferens.

### Educational objective:

Hemorrhoids result from abnormal distension of a portion of the anal arteriovenous plexus. The vascular components of internal hemorrhoids drain into the superior rectal vein, which subsequently drains into the inferior mesenteric vein. Band ligation of hemorrhoids cuts off their blood supply, causing them to degenerate.

### References

- [Hemorrhoids.](#)

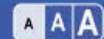




An 8-year-old boy with acute lymphoblastic leukemia receiving maintenance chemotherapy is hospitalized due to fever and neutropenia. Treatment with broad spectrum intravenous antibiotics is begun and the patient's fever resolves. His neutrophil count increases with granulocyte colony-stimulating factor therapy and blood cultures remain negative. On day 5 of hospitalization, the patient experiences nausea, abdominal cramping, and 6-8 episodes of watery diarrhea. Temperature is 37.7 C (100 F). Physical examination shows mild lower abdominal tenderness without guarding or rebound tenderness. Stool testing for occult blood is negative. Which of the following is the single best stool test to establish the cause of this patient's diarrhea?

- ☐ A. Culture on sorbitol-MacConkey agar
- ☐ B. Enzyme immunoassay for bacterial antigen
- ☐ C. Latex agglutination for viral antigens
- ☐ D. Microscopy after modified acid-fast staining
- ☐ E. Microscopy for ova and parasites
- ☐ F. PCR for bacterial gene encoding a toxin





patient's fever resolves. His neutrophil count increases with granulocyte colony-stimulating factor therapy and blood cultures remain negative. On day 5 of hospitalization, the patient experiences nausea, abdominal cramping, and 6-8 episodes of watery diarrhea. Temperature is 37.7 C (100 F). Physical examination shows mild lower abdominal tenderness without guarding or rebound tenderness. Stool testing for occult blood is negative. Which of the following is the single best stool test to establish the cause of this patient's diarrhea?

- ☐ A. Culture on sorbitol-MacConkey agar (5%)
- ☐ B. Enzyme immunoassay for bacterial antigen (17%)
- ☐ C. Latex agglutination for viral antigens (3%)
- ☐ D. Microscopy after modified acid-fast staining (3%)
- ☐ E. Microscopy for ova and parasites (5%)
- ☒ F. PCR for bacterial gene encoding a toxin (64%)

Correct



64%

Answered correctly



16 secs

Time spent



02/11/2021

Last updated

Block Time Remaining: 00:18:00

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End Block





This child who developed diarrhea, nausea, and abdominal cramping while on antibiotics should be tested for ***Clostridium difficile* infection** (CDI). Patients who develop acute diarrhea ( $\geq 3$  loose stool in 24 hours), particularly those with risk factors (eg, hospitalization, antibiotic use), should have stool samples sent for evaluation.

Diagnostic testing includes:

- **Nucleic acid amplification test (NAAT):** Uses a **polymerase chain reaction** to detect genes present in toxigenic strains (eg, **toxin B-encoding gene**). This test is **highly sensitive and specific** for toxigenic strains but does not distinguish active toxin production and may lead to overdiagnosis in asymptomatic carriers.
- **Enzyme immunoassays (EIA):** Uses antibodies to detect *C difficile* antigens or toxins. EIA for bacterial toxins is highly specific but has **poor sensitivity** as large amounts of toxin are required. In contrast, EIA for glutamate dehydrogenase (a bacterial antigen expressed by all *C difficile* isolates) has better sensitivity but cannot distinguish toxin-producing strains.

NAAT is considered the most sensitive method for diagnosis of CDI in patients with clinical symptoms. EIA for bacterial toxins can be added as part of a multistep algorithm to increase specificity of active disease; however, it is not recommended for use alone. (Choice B)





NAAT is considered the most sensitive method for diagnosis of CDI in patients with clinical symptoms. EIA for bacterial toxins can be added as part of a multistep algorithm to increase specificity of active disease; however, it is not recommended for use alone (**Choice B**).

(**Choice A**) Culture on sorbitol-MacConkey agar is used to diagnose *Escherichia coli* O157:H7 (ie, enterohemorrhagic *E coli* [EHEC]). EHEC presents with bloody diarrhea; this patient's nonbloody diarrhea and recent antibiotic exposure makes CDI more likely.

(**Choice C**) Latex agglutination for viral antigens is used to diagnose rotavirus, which causes nonbloody diarrhea, vomiting, and fever; disease can be particularly severe in immunocompromised patients. However, incubation time is typically <48 hours, and it is unlikely that this patient would develop an infection after 5 days in the hospital.

(**Choice D**) Modified acid-fast staining is used to diagnose cryptosporidium infection, which causes chronic diarrhea (particularly in HIV-infected patients). This patient's current hospitalization and antibiotic use make CDI more likely.

(**Choice E**) Stool ova and parasites are used to diagnose intestinal parasites (eg, *Giardia*, *Entamoeba*). These can cause diarrhea, which can be particularly severe in immunocompromised patients, but are unlikely to occur after 5 days in the hospital. *Entamoeba histolytica* typically presents with bloody stool





diarrhea, vomiting, and fever; disease can be particularly severe in immunocompromised patients.

However, incubation time is typically <48 hours, and it is unlikely that this patient would develop an infection after 5 days in the hospital.

**(Choice D)** Modified acid-fast staining is used to diagnose cryptosporidium infection, which causes chronic diarrhea (particularly in HIV-infected patients). This patient's current hospitalization and antibiotic use make CDI more likely.

**(Choice E)** Stool ova and parasites are used to diagnose intestinal parasites (eg, *Giardia*, *Entamoeba*). These can cause diarrhea, which can be particularly severe in immunocompromised patients, but are unlikely to occur after 5 days in the hospital. *Entamoeba histolytica* typically presents with bloody stool after travel to resource-limited countries.

### Educational objective:

*Clostridium difficile* commonly presents with diarrhea and abdominal pain; hospitalization and antibiotic use increase the risk of contracting the disease. A nucleic acid amplification test is considered the most sensitive method for diagnosis of *C difficile* infection in patients with clinical symptoms.

Microbiology      Gastrointestinal & Nutrition      Clostridium difficile infection  
 Subject              System                              Topic

Block Time Remaining: 00:18:00

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Feedback

Suspend

End Block





A 6-year-old boy is brought to the ER due to confusion and intractable vomiting. These symptoms began a few hours ago and have been gradually worsening. The patient's mother tells you that the boy contracted a febrile illness from his younger brother two days ago. She states that she gave him "some over-the-counter pills" and it helped his fever. While you talk to the mother, the boy lapses into a coma. The light microscopy of his liver specimen will reveal:

- ☐ A. Apoptosis of hepatocytes
- ☐ B. Periportal inflammatory infiltration
- ☐ C. Microvesicular steatosis
- ☐ D. Centrilobular congestion
- ☐ E. Bile duct proliferation

Submit





A 6-year-old boy is brought to the ER due to **confusion** and intractable vomiting. These symptoms began a few hours ago and have been gradually worsening. The patient's mother tells you that the boy contracted a febrile illness from his younger brother two days ago. She states that she gave him "some over-the-counter pills" and it helped his fever. While you talk to the mother, the boy lapses into a coma. The light microscopy of his liver specimen will reveal:

- ☐ A. Apoptosis of hepatocytes (25%)
- ☐ B. Periportal inflammatory infiltration (15%)
- ☒ C. Microvesicular steatosis (46%)
- ☐ D. Centrilobular congestion (12%)
- ☐ E. Bile duct proliferation (0%)

Correct



46%  
Answered correctly



18 secs  
Time Spent



09/30/2020  
Last Updated





Children with febrile illness treated with salicylates are at risk of developing Reye syndrome. Reye syndrome is characterized by hepatic failure and acute encephalopathy, and is most commonly associated with the use of **aspirin** in patients 5-14 years old. The febrile illness that preceeds Reye's syndrome is frequently an upper respiratory infection, influenza, measles, varicella or another viral disease. The pathogenesis of this condition is still unclear, but it is hypothesized that affected children have some inborn metabolic error that renders them sensitive to the toxic effects of salicylates. It is especially pronounced in viral-infected cells and causes mitochondrial dysfunction. The two components of Reye's syndrome include:

1. **Hepatic dysfunction** manifests with vomiting and hepatomegaly, but jaundice is rare. Liver function tests reveal increased levels of ALT, AST, ammonia, and bilirubin, and a prolonged PT and PTT. Light microscopy of a liver biopsy shows microvesicular steatosis, the presence of small fat vacuoles in the cytoplasm of hepatocytes (**Choice C**). No necrosis or inflammation is present in the liver. Electron microscopy findings include swelling, a decreased number of mitochondria and glycogen depletion.
2. **Encephalopathy** of Reye syndrome is attributed to hepatic dysfunction and the toxic effect of hyperammonemia on the CNS leading to cerebral edema.







2. **Encephalopathy** of Reye syndrome is attributed to hepatic dysfunction and the toxic effect of hyperammonemia on the CNS leading to cerebral edema.

To avoid the possibility of inducing Reye syndrome, aspirin should not be administered to children under the age of sixteen except for very specific circumstances where it is indicated for the treatment of a serious illness such as in Kawasaki disease where salicylates are a mainstay of treatment.

**(Choices A and B)** Apoptosis of hepatocytes, acinar necrosis and periportal mononuclear inflammatory infiltration are the characteristic light microscopy findings of viral hepatitis caused by any of the hepatitis viruses.

**(Choice D)** Centrilobular congestion occurs in the liver of the patients with right-sided heart failure.

**(Choice E)** Primary biliary cirrhosis displays bile duct destruction, periductal granulomatous inflammation and bile duct proliferation.

**Educational Objective:**

Reye syndrome occurs in children with febrile illness treated with salicylates (**aspirin**). It consists of hepatic failure and encephalopathy. The characteristic histological finding is microvesicular steatosis of hepatocytes without inflammation and cerebral edema.





A 38-year-old man comes to the office with abdominal discomfort and loose stools over the past year. He has also lost 10 kg (22 lb) despite having a normal appetite. The patient eats a balanced diet that includes a variety of fruits and vegetables, meats, whole grains, and dairy products. He has had no international travel, works indoors as an office manager, and has no sick contacts. Medical history is insignificant and the patient takes no medications. The patient drinks alcohol socially and does not use tobacco. Vital signs and physical examination are normal. Serum chemistry panel, complete blood count, and thyroid function tests are normal. Which of the following is the best next step for assessing for impaired nutrient absorption in this patient?

- ☐ A. Abdominal ultrasound
- ☐ B. Colonoscopy
- ☐ C. Jejunal biopsy
- ☒ D. Stool evaluation for ova and parasites
- ☐ E. Stool microscopy with Sudan III stain
- ☐ F. Vitamin B<sub>12</sub> level





a variety of fruits and vegetables, meats, whole grains, and dairy products. He has had no international travel, works indoors as an office manager, and has no sick contacts. Medical history is insignificant and the patient takes no medications. The patient drinks alcohol socially and does not use tobacco. Vital signs and physical examination are normal. Serum chemistry panel, complete blood count, and thyroid function tests are normal. Which of the following is the best next step for assessing for impaired nutrient absorption in this patient?

- ☐ A. Abdominal ultrasound (4%)
- ☐ B. Colonoscopy (19%)
- ☐ C. Jejunal biopsy (29%)
- ☐ D. Stool evaluation for ova and parasites (9%)
- ☒ E. Stool microscopy with Sudan III stain (27%)
- ☐ F. Vitamin B<sub>12</sub> level (9%)

Correct



27%



02 mins, 02 secs

Time Spent



12/02/2020

Last Updated

Block Time Remaining: 00:20:20

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Feedback



Suspend



End Block





Impaired intestinal absorption of nutrients is called **malabsorption**. Significant malabsorption may present with diarrhea and **steatorrhea** (bulky, foul-smelling stools; visible oil droplets; greasy toilet ring), but more often patients have nonspecific symptoms such as weight loss, fatigue, or vague abdominal discomfort. Patients may also have characteristic findings due to **specific nutrient deficiencies**. Generalized malabsorption is commonly due to defects in pancreatic secretion (eg, chronic pancreatitis, cystic fibrosis), mucosal disorders (eg, celiac disease, inflammatory bowel disease), bacterial overgrowth (eg, gastrointestinal surgery, abnormal motility), or parasitic diseases (eg, *Giardia*).

Dietary lipids are the macronutrient with the most complex digestive pathway. Fats are typically the earliest and most severely affected nutrient in generalized malabsorption, and **testing for fat** malabsorption is therefore the **most sensitive** strategy for screening for malabsorptive disorders. A qualitative assay of stool with **Sudan III stain** can quickly and easily identify unabsorbed fat and confirm malabsorption. (Stool should normally contain no measurable fat.)

**(Choices A, B, C, and D)** Abdominal imaging can be used to identify thickening of the bowel wall due to inflammation or structural disorders of the pancreas (eg, chronic pancreatitis). Endoscopy with jejunal biopsy can diagnose celiac disease, and colonoscopy can identify inflammatory bowel disease. Stool inspection for ova and parasites can identify infectious causes of malabsorption such as *Giardia* and

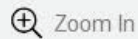




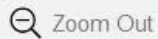
## Exhibit Display

**Nutrient deficiencies associated with malabsorption**

Nutrient	Clinical presentation
Protein	Muscle wasting, edema
Fat	Weight loss
Iron Folate Vitamin B <sub>12</sub>	Anemia
Calcium Vitamin D	Bone pain, muscle weakness, tetany
Vitamin A	Hyperkeratosis, night blindness
Vitamin K	Petechiae, easy bruising



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**(Choices A, B, C, and D)** Abdominal imaging can be used to identify thickening of the bowel wall due to inflammation or structural disorders of the pancreas (eg, chronic pancreatitis). Endoscopy with jejunal biopsy can diagnose celiac disease, and colonoscopy can identify inflammatory bowel disease. Stool inspection for ova and parasites can identify infectious causes of malabsorption such as *Giardia* and *Cryptosporidium*. Although these tests are useful for determining **specific causes** of generalized malabsorption, fecal fat testing is a less invasive and more sensitive test for confirming malabsorption of any etiology.

**(Choice F)** Iron and vitamin B<sub>12</sub> deficiency occur commonly in patients with malabsorption. However, vitamin B<sub>12</sub> levels have a low sensitivity for malabsorption; deficiency develops only after years and is more common with specific etiologies (eg, pernicious anemia). In addition, this patient's normal complete blood count makes vitamin B<sub>12</sub> deficiency less likely.

### Educational objective:

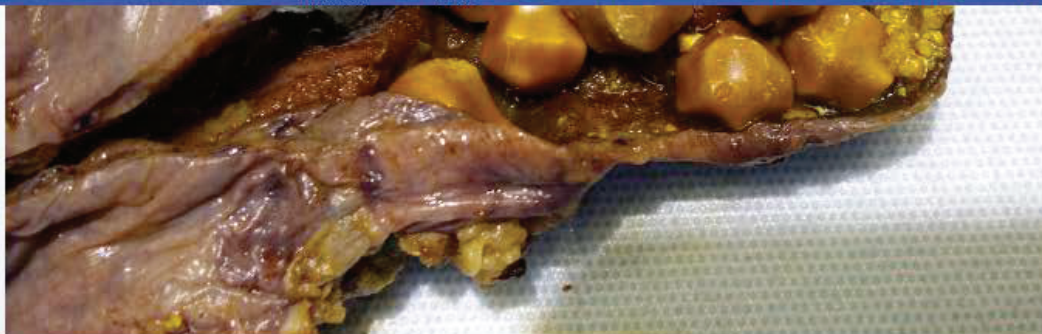
Malabsorption is a syndrome of impaired intestinal digestion and absorption. Fats are typically the most severely affected macronutrient in generalized malabsorption, and testing the stool for fat (eg, with Sudan III stain) is the most sensitive strategy for screening for malabsorptive disorders.





A 40-year-old woman comes to the office due to recurrent episodes of postprandial abdominal pain. The pain is in the right upper quadrant and is associated with nausea. The patient has no fever, jaundice, or loss of appetite. Other medical conditions include obstructive sleep apnea and obesity. The patient takes no medications. She has never had any surgeries. She does not use tobacco, alcohol, or illicit drugs. The patient is afebrile. Blood pressure is 140/90 mm Hg. BMI is 38 kg/m<sup>2</sup>. Examination shows tenderness in the right upper quadrant. Abdominal ultrasound demonstrates multiple gallstones. A gross specimen obtained from laparoscopic cholecystectomy is shown in the image below:





Which of the following is the most likely mechanism responsible for gallstone formation in this patient?

- ☐ A. Altered enterohepatic cycling of bilirubin
- ☐ B. Decreased bile acid synthesis
- ☐ C. Delayed gallbladder emptying
- ☐ D. Increased cholesterol synthesis
- ☐ E. Increased efflux of bilirubin into bile

Submit

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End Block



Which of the following is the most likely mechanism responsible for gallstone formation in this patient?

- ☐ A. Altered enterohepatic cycling of bilirubin (1%)
- ☒ B. Decreased bile acid synthesis (9%)
- ☐ C. Delayed gallbladder emptying (13%)
- ☒ D. Increased cholesterol synthesis (73%)
- ☐ E. Increased efflux of bilirubin into bile (1%)

Incorrect

Correct answer



73%



01 min, 53 secs

Time spent



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Bile is stored and concentrated within the gallbladder and is involved in digestion and absorption of dietary fats and removal of waste products (eg, bilirubin, cholesterol) for excretion in feces. Gallstones usually occur when one such waste product supersaturates the bile, resulting in precipitation and eventual stone formation.

In the United States, most gallstones are due to the **supersaturation of cholesterol**, which usually precipitates out of bile with calcium salts and mucin, forming **white or yellow cholesterol stones**, as seen in this patient. **Cholesterol stone** formation occurs due to the following:

- **Increased cholesterol synthesis:** Hypercholesterolemia, caused by diet, genetics, diabetes mellitus, medications (eg, oral contraceptives), or **obesity** (increased HMG-CoA reductase activity), results in hypersecretion of cholesterol into the bile.
- **Gallbladder hypomotility:** Pregnancy, medications (eg, somatostatin), prolonged fasting, parenteral nutrition, and spinal cord injury lead to **gallbladder stasis**, which promotes excessive water resorption from bile and concentration of cholesterol.
- **Decreased bile acid synthesis** (or recirculation): Fibrates (eg, fenofibrate) inhibit bile acid synthesis, increasing cholesterol concentration within the bile. Decreased bile acid resorption at the ileum (eg, due to Crohn disease) also promotes cholesterol concentration.





- **Decreased bile acid synthesis** (or recirculation): Fibrates (eg, fenofibrate) inhibit bile acid synthesis, increasing cholesterol concentration within the bile. Decreased bile acid resorption at the ileum (eg, due to Crohn disease) also promotes cholesterol concentration.
- Increased calcium or mucin concentration: Rapid weight loss (eg, gastric bypass) promotes increased calcium and mucin concentrations in the bile, which trap cholesterol crystals and promote stone formation.

**(Choices A and E)** Increased enterohepatic cycling of bilirubin occurs with ileal disease (eg, Crohn disease), as the loss of bile acids promotes reabsorption of unconjugated bilirubin. Increased efflux of bilirubin into bile also occurs with hyperbilirubinemia from chronic hemolysis (eg, sickle cell disease). Because of high bilirubin concentrations, these mechanisms promote the formation of black pigment stones, not cholesterol stones.

**(Choices B and C)** Although both decreased bile acid synthesis (eg, due to fibrate medications) and gallbladder hypomotility (eg, due to pregnancy, prolonged fasting, or spinal cord injury) promote the formation of cholesterol gallstones, this patient does not have risk factors for either etiology.

### Educational objective:

Most gallstones occur due to the supersaturation of cholesterol, which precipitates out of bile with mucin







**(Choices A and E)** Increased enterohepatic cycling of bilirubin occurs with ileal disease (eg, Crohn disease), as the loss of bile acids promotes reabsorption of unconjugated bilirubin. Increased efflux of bilirubin into bile also occurs with hyperbilirubinemia from chronic hemolysis (eg, sickle cell disease). Because of high bilirubin concentrations, these mechanisms promote the formation of black **pigment stones**, not cholesterol stones.

**(Choices B and C)** Although both decreased bile acid synthesis (eg, due to fibrate medications) and gallbladder hypomotility (eg, due to pregnancy, prolonged fasting, or spinal cord injury) promote the formation of cholesterol gallstones, this patient does not have risk factors for either etiology.

### Educational objective:

Most gallstones occur due to the supersaturation of cholesterol, which precipitates out of bile with mucin and calcium salts to form white or yellow cholesterol stones. Factors that promote the formation of cholesterol stones include increased cholesterol synthesis, gallbladder hypomotility, increased calcium or mucin concentration, and decreased bile acid synthesis or recirculation.

Pathology

Gastrointestinal &amp; Nutrition

Gallstone disease

Subject

System

Topic







A 32-year-old man comes to the clinic for peptic ulcer disease follow-up. The patient has received several months of proton pump inhibitor therapy without significant improvement in his epigastric discomfort. He does not use nonsteroidal anti-inflammatory drugs, tobacco, or alcohol. *Helicobacter pylori* testing is negative. The patient undergoes a partial gastrectomy for refractory peptic ulcer disease. The pathologist receives the tissue and notes significant enlargement of the gastric rugal folds on gross examination. Microscopy of the gastric mucosa reveals parietal cell hyperplasia. Which of the following stimuli is the most likely cause of parietal cell proliferation in this patient?

- ☐ A. Acetylcholine
- ☐ B. Gastrin
- ☐ C. Secretin
- ☐ D. Serotonin
- ☐ E. Somatostatin
- ☐ F. Transforming growth factor alpha





months of proton pump inhibitor therapy without significant improvement in his epigastric discomfort. He does not use nonsteroidal anti-inflammatory drugs, tobacco, or alcohol. *Helicobacter pylori* testing is negative. The patient undergoes a partial gastrectomy for refractory peptic ulcer disease. The pathologist receives the tissue and notes significant enlargement of the gastric rugal folds on gross examination. Microscopy of the gastric mucosa reveals parietal cell hyperplasia. Which of the following stimuli is the most likely cause of parietal cell proliferation in this patient?

- ☐ A. Acetylcholine (7%)
- ☒ B. Gastrin (82%)
- ☐ C. Secretin (3%)
- ☐ D. Serotonin (0%)
- ☐ E. Somatostatin (1%)
- ☐ F. Transforming growth factor alpha (3%)

Correct

82%



14 secs



12/27/2020

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End Block



**Parietal cells** are located in the gastric glands of the fundus and body of the stomach. They can be spotted easily due to their eosinophilic cytoplasm on H&E stain. These cells have abundant mitochondria and an intracellular tubulovesicular system that allows them to secrete large quantities of gastric acid (HCl) and intrinsic factor.

Parietal cells are influenced by a number of substances. Histamine, acetylcholine, and gastrin increase gastric acid secretion, but prostaglandins inhibit it. **Gastrin** not only stimulates **HCl secretion**, but it also has a **trophic effect** on parietal cells. In patients with Zollinger-Ellison syndrome (such as this patient), gastrin hypersecretion induces **parietal cell hyperplasia**, causing visible **enlargement of gastric folds** on endoscopy. The increased gastric acid secretion induced by excess gastrin also causes peptic ulcer disease, heartburn, and diarrhea.

**(Choice A)** Acetylcholine is a universal neurotransmitter that is present in parasympathetic postganglionic synapses and in all autonomic preganglionic synapses. Cholinergic receptors are divided into muscarinic (located in smooth muscle and glands) and nicotinic (found at the neuromuscular junction). Acetylcholine stimulates parietal cell acid secretion but is not typically associated with parietal cell hyperplasia or gastric fold enlargement.

**(Choice C)** Secretin is produced by S cells of the small intestine. It increases bicarbonate production by







stimulates parietal cell acid secretion but is not typically associated with parietal cell hyperplasia or gastric fold enlargement.

**(Choice C)** Secretin is produced by S cells of the small intestine. It increases bicarbonate production by the pancreas and leads to the secretion of watery, alkaline pancreatic juice. This substance also inhibits gastric acid secretion and stimulates pyloric sphincter contraction.

**(Choice D)** Serotonin (5HT) is primarily found in enterochromaffin cells of the gastrointestinal (GI) tract, the central nervous system, and platelets. In the GI tract, it helps to regulate intestinal secretions and peristalsis.

**(Choice E)** Somatostatin (growth hormone-inhibiting hormone) is secreted by D cells of pancreatic islets and GI mucosa. It has multiple inhibitory effects over the GI tract, including decreasing motility, gastrin secretion, pancreatic endocrine/exocrine secretion, and absorption of nutrients.

**(Choice F)** Transforming growth factor alpha (TGF- $\alpha$ ) is a potent stimulator of epithelial growth and is secreted by carcinomas, macrophages, and epithelial cells. Menetrier disease is associated with overproduction of TGF- $\alpha$ , resulting in mucosal-cell hyperplasia with gastric fold enlargement. However, the condition causes hypoplasia of parietal/chief cells, resulting in glandular atrophy with reduced gastric acid secretion.





**(Choice E)** Somatostatin (growth hormone-inhibiting hormone) is secreted by D cells of pancreatic islets and GI mucosa. It has multiple inhibitory effects over the GI tract, including decreasing motility, gastrin secretion, pancreatic endocrine/exocrine secretion, and absorption of nutrients.

**(Choice F)** Transforming growth factor alpha (TGF- $\alpha$ ) is a potent stimulator of epithelial growth and is secreted by carcinomas, macrophages, and epithelial cells. Menetrier disease is associated with overproduction of TGF- $\alpha$ , resulting in mucosal-cell hyperplasia with gastric fold enlargement. However, the condition causes hypoplasia of parietal/chief cells, resulting in glandular atrophy with reduced gastric acid secretion.

### Educational objective:

Patients with Zollinger-Ellison syndrome develop peptic ulcer disease and parietal cell hyperplasia with gastric fold enlargement due to gastrin hypersecretion.

### References

- [Zollinger-Ellison Syndrome.](#)
- [Role of gastrointestinal hormones in the proliferation of normal and neoplastic tissues.](#)





A 68-year-old woman comes to the emergency department due to shortness of breath, poor appetite, and abdominal distension for the past 3 months. Her symptoms have progressively worsened, and now she is unable to perform her daily activities. The patient has a history of coronary artery disease and underwent coronary artery bypass grafting 3 years ago. She also has myelodysplastic syndrome for which she receives intermittent blood transfusions. Physical examination shows jugular venous distension, abdominal distension, hepatomegaly, and lower extremity edema. A representative liver biopsy image is shown in the [exhibit](#). Which of the following is the most likely cause of this patient's liver findings?

- ☐ A. Autoimmune biliary destruction
- ☐ B. Excessive deposition of iron
- ☐ C. Hepatitis virus infection
- ☐ D. Metastatic spread to the liver
- ☐ E. Passive hepatic congestion

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Item 23 of 40  
Question Id: 15535



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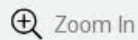
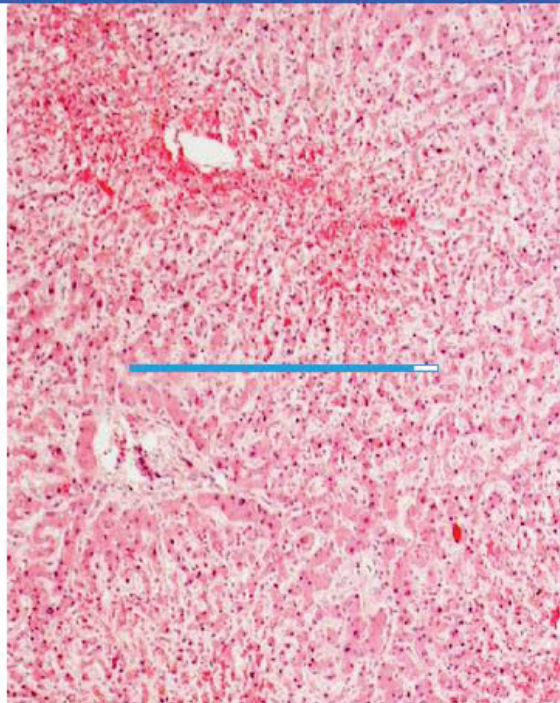


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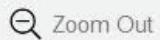


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A 68-year-old woman comes to the emergency department due to shortness of breath, poor appetite, and abdominal distension for the past 3 months. Her symptoms have progressively worsened, and now she is unable to perform her daily activities. The patient has a history of coronary artery disease and underwent coronary artery bypass grafting 3 years ago. She also has myelodysplastic syndrome for which she receives intermittent **blood transfusions**. Physical examination shows jugular venous distension, abdominal distension, hepatomegaly, and lower extremity edema. A representative liver biopsy image is shown in the [exhibit](#). Which of the following is the most likely cause of this patient's liver findings?

- ☐ A. Autoimmune biliary destruction (3%)
- ☒ B. Excessive deposition of iron (26%)
- ☐ C. Hepatitis virus infection (8%)
- ☐ D. Metastatic spread to the liver (2%)
- ☒ E. Passive hepatic congestion (58%)

Incorrect

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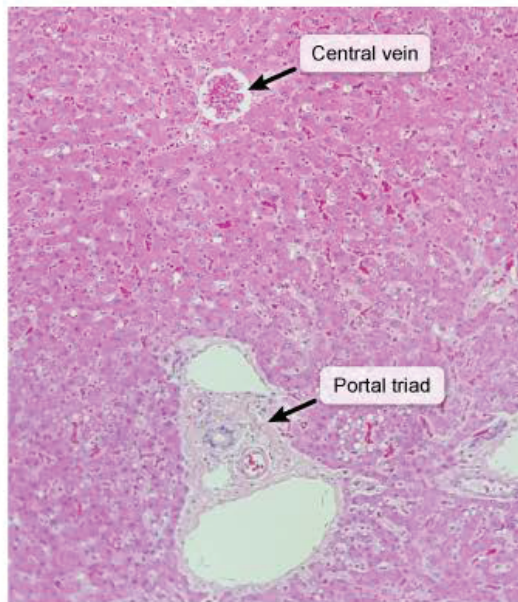
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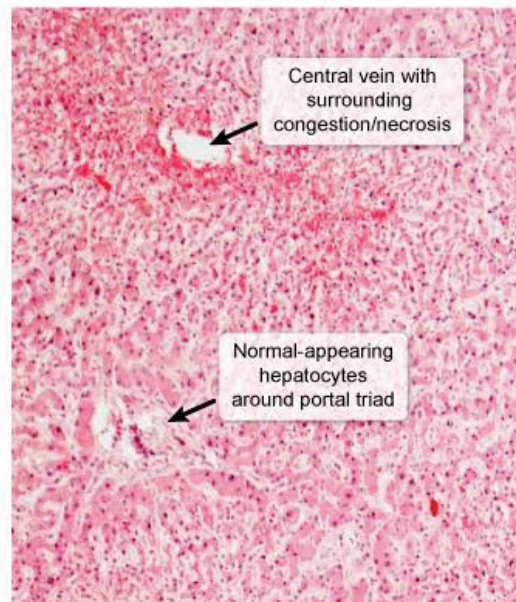
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Normal liver



Congestive hepatopathy



This patient's shortness of breath—accompanied by abdominal distension (ascites), hepatomegaly, jugular







©UWorld

This patient's shortness of breath—accompanied by abdominal distension (ascites), hepatomegaly, jugular venous distension, and lower extremity edema—is consistent with **right-sided heart failure**; her liver biopsy demonstrates evidence of **congestive hepatopathy**.

In congestive hepatopathy, outflow of blood from the hepatic veins is impeded by elevated right atrial and vena caval pressures, which leads to **increased hydrostatic pressure** in the central veins of the liver. There is consequent seepage of fluid into the surrounding hepatocytes with resulting congestion and hepatic necrosis. The hepatocellular damage favors the centrilobular areas (**zone 3**) where congestion is most prominent. On microscopy, patchy hemorrhage is seen surrounding the central veins consistent with **centrilobular necrosis**. These areas of necrosis contrast with the relatively normal-appearing hepatocytes in the periportal regions (zone 1), creating an overall heterogenous appearance sometimes referred to as "**nutmeg liver**."

In addition to signs and symptoms of right-sided heart failure, patients with congestive hepatopathy may have localized right upper quadrant pain (due to stretching of the hepatic capsule), and laboratory results may demonstrate modest elevations in serum bilirubin and transaminases.

**(Choice A)** Autoimmune destruction of intrahepatic biliary ducts occurs in primary biliary cholangitis





**(Choice A)** Autoimmune destruction of intrahepatic biliary ducts occurs in primary biliary cholangitis (formerly primary biliary cirrhosis). Because intrahepatic bile ducts are concentrated in the periportal regions, histopathology demonstrates **periductal fibrosis** predominantly in those regions.

**(Choice B)** Excessive hepatic deposition of iron most commonly occurs due to hemochromatosis. Patients receiving frequent blood transfusions are also at risk; however, histopathology would demonstrate periportal fibrosis and numerous **brown pigments** representing iron deposits. Fibrosis favors the periportal regions likely because those hepatocytes are exposed to the highest concentrations of iron-rich blood coming from the portal vein.

**(Choice C)** Histopathology in chronic viral hepatitis (eg, chronic hepatitis C) reveals dense infiltrate of **mononuclear inflammatory cells** in the periportal regions; there is often gradual development of periportal fibrosis that may eventually bridge to the centrilobular regions.

**(Choice D)** Histopathology of metastatic spread to the liver is unlikely to demonstrate a consistent pattern of lobular necrosis, but it can reveal an abrupt **demarcation** between normal hepatocellular tissue and the metastatic tumor.

**Educational objective:**

Congestive hepatopathy is a common complication of right-sided heart failure. Patchy hemorrhage and







Patients receiving frequent blood transfusions are also at risk; however, histopathology would demonstrate periportal fibrosis and numerous **brown pigments** representing iron deposits. Fibrosis favors the periportal regions likely because those hepatocytes are exposed to the highest concentrations of iron-rich blood coming from the portal vein.

**(Choice C)** Histopathology in chronic viral hepatitis (eg, chronic hepatitis C) reveals dense infiltrate of **mononuclear inflammatory cells** in the periportal regions; there is often gradual development of periportal fibrosis that may eventually bridge to the centrilobular regions.

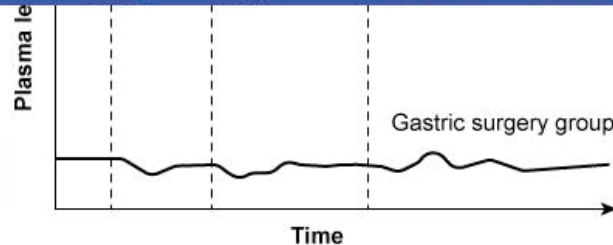
**(Choice D)** Histopathology of metastatic spread to the liver is unlikely to demonstrate a consistent pattern of lobular necrosis, but it can reveal an abrupt **demarcation** between normal hepatocellular tissue and the metastatic tumor.

### Educational objective:

Congestive hepatopathy is a common complication of right-sided heart failure. Patchy hemorrhage and necrosis predominantly affect the centrilobular regions (zone 3) where hepatic congestion is most prominent. The centrilobular necrosis, combined with relatively normal-appearing periportal regions (zone 1), creates an overall heterogenous appearance sometimes referred to as "nutmeg liver."





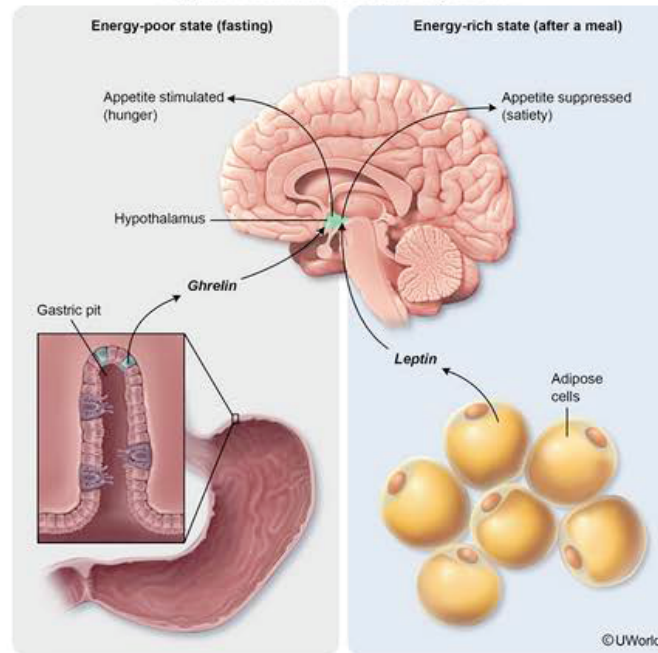


This profile most likely represents which of the following hormones?

- ☐ A. Cholecystokinin (3%)
- ☐ B. Gastrin (21%)
- ☒ C. Ghrelin (63%)
- ☐ D. Insulin (4%)
- ☐ E. Leptin (4%)
- ☐ F. Motilin (1%)

### Exhibit Display

#### Appetite hormones: leptin & ghrelin



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The 24-hour hormone levels in the control subjects show increasing secretion leading up to meals, followed by a sharp postprandial drop. However, the subjects who have undergone gastrectomy show lower baseline levels with attenuation of meal-related fluctuations. This pattern suggests that the hormone is likely secreted in the stomach and suppressed by food intake, which is consistent with the secretory pattern of **ghrelin**.

Ghrelin is **produced primarily in the stomach** in response to **fasting**; levels surge leading up to meals and fall after eating. Ghrelin **stimulates appetite** and promotes **weight gain**. Caloric restriction and falling fat stores lead to increased ghrelin levels (along with decreased leptin and insulin levels), which limits weight loss from dietary modification alone. However, patients who have undergone **bariatric procedures** that remove a portion of the stomach (eg, roux-en-Y gastric bypass, sleeve **gastrectomy**) can lose a significant number of ghrelin-secreting cells. This leads to **lower ghrelin levels** and less stimulation of appetite in response to fasting, promoting weight loss.

**(Choice A)** Cholecystokinin stimulates gallbladder contraction and pancreatic enzyme and bicarbonate secretion. It is secreted in the duodenum and jejunum in response to fat and protein in the intestinal lumen, and levels rise following meals.





Mark

Previous

Next

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Tutorial

Lab Values

Notes

Calculator

Reverse Color

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appetite in response to fasting, promoting weight loss.

**(Choice A)** Cholecystokinin stimulates gallbladder contraction and pancreatic enzyme and bicarbonate secretion. It is secreted in the duodenum and jejunum in response to fat and protein in the intestinal lumen, and levels rise following meals.

**(Choice B)** Gastrin stimulates parietal cell acid production. It is secreted primarily by G cells of the gastric antrum in response to vagal activity, gastric distension, and the presence of amino acids in the gastric lumen. Although gastrin production would be lower in the postgastrectomy subjects, gastrin levels normally rise (not fall) in response to meals.

**(Choice D)** Insulin levels rise rapidly in response to increased blood glucose following meals then gradually fall back to baseline. Insulin is secreted by pancreatic beta cells and would not be drastically reduced following gastrectomy.

**(Choice E)** Leptin is produced primarily by fat cells in response to short-term food intake and long-term adequacy of fat stores. It acts on the hypothalamus to decrease appetite (obesity blunts this action). During fasting states, leptin levels fall.

**(Choice F)** Motilin stimulates smooth muscle contraction in the upper gastrointestinal tract and generally



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gradually fall back to baseline. Insulin is secreted by pancreatic beta cells and would not be drastically reduced following gastrectomy.

**(Choice E)** Leptin is produced primarily by fat cells in response to short-term food intake and long-term adequacy of fat stores. It acts on the hypothalamus to decrease appetite (obesity blunts this action). During fasting states, leptin levels fall.

**(Choice F)** Motilin stimulates smooth muscle contraction in the upper gastrointestinal tract and generally increases gastric motility. Although secretion appears to increase during fasting and decrease following meals, it is produced primarily in the duodenal mucosa rather than the stomach.

### Educational objective:

Ghrelin is produced in the stomach in response to fasting; levels surge leading up to meals and fall after eating. Ghrelin stimulates appetite and promotes weight gain. Patients who have undergone gastrectomy have reduced ghrelin levels, leading to weight loss.

### References

- [The impact of laparoscopic sleeve gastrectomy on plasma ghrelin levels: a systematic review.](#)

Pharmacology

Gastrointestinal & Nutrition

Obesity



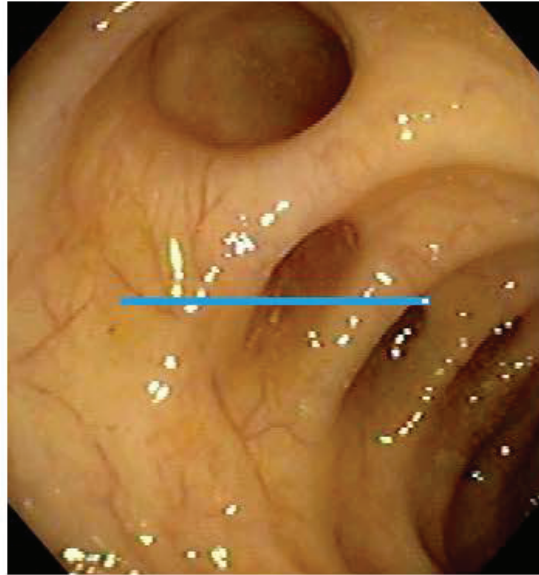
A 72-year-old woman comes to the emergency department due to bloody bowel movements. One hour ago, the patient had a sudden urge to defecate and passed a large amount of bright red blood mixed with stool. Several minutes later, she had another episode with a small amount of blood. The patient reports no nausea, vomiting, abdominal pain, diarrhea, or fever and never had such symptoms before. She is hospitalized but has no further bleeding. Physical examination, including a digital rectal examination, is unremarkable. A colonoscopy performed after bowel preparation reveals the findings in the [exhibit](#). There are no other abnormalities. Which of the following is the most likely source of this patient's bleeding?

- ☐ A. Abnormal arteriovenous channel
- ☐ B. Diffusely eroded mucosal surface
- ☐ C. Dilated and tortuous venous plexus
- ☐ D. Disruption of vasa recta
- ☐ E. Sloughed off polypoidal mass

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Exhibit Display



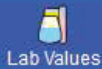
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A 72-year-old woman comes to the emergency department due to bloody bowel movements. One hour ago, the patient had a sudden urge to defecate and passed a large amount of bright red blood mixed with stool. Several minutes later, she had another episode with a small amount of blood. The patient reports no nausea, vomiting, abdominal pain, diarrhea, or fever and never had such symptoms before. She is hospitalized but has no further bleeding. Physical examination, including a digital rectal examination, is unremarkable. A colonoscopy performed after bowel preparation reveals the findings in the [exhibit](#). There are no other abnormalities. Which of the following is the most likely source of this patient's bleeding?

- ☐ A. Abnormal arteriovenous channel (6%)
- ☐ B. Diffusely eroded mucosal surface (17%)
- ☐ C. Dilated and tortuous venous plexus (7%)
- ☒ D. Disruption of vasa recta (63%)
- ☐ E. Sloughed off polypoidal mass (4%)



### Diverticular disease

<b>Etiology</b>	<ul style="list-style-type: none"><li>• Diverticulosis: ↑ intraluminal pressure causing herniation through points of weakness (vasa recta penetration)</li><li>• Diverticular bleeding: injury to exposed vasa recta</li><li>• Diverticulitis: trapped food particles &amp; ↑ intraluminal pressure causing microperforation</li></ul>
<b>Symptoms</b>	<ul style="list-style-type: none"><li>• Diverticulosis: none</li><li>• Diverticular bleeding: painless hematochezia</li><li>• Diverticulitis: left lower quadrant pain, nausea, vomiting, fever</li></ul>
<b>Risk factors</b>	<ul style="list-style-type: none"><li>• Diet high in red meat &amp; fat &amp; low in fiber</li><li>• Obesity, physical inactivity, smoking</li></ul>

This patient with hematochezia had a colonoscopy revealing multiple outpouchings of the colonic mucosa, consistent with **colonic diverticulosis**. The incidence of diverticulosis increases with age and is seen typically in patients age >60. Risk factors include low-fiber, high-fat diet, obesity, and physical inactivity.



**factors**

- Obesity, physical inactivity, smoking

This patient with hematochezia had a colonoscopy revealing multiple outpouchings of the colonic mucosa, consistent with **colonic diverticulosis**. The incidence of diverticulosis increases with age and is seen typically in patients age >60. Risk factors include low-fiber, high-fat diet, obesity, and physical inactivity.

Diverticula tend to form in areas where the intraluminal colon wall lacks structural integrity. Typically, these weak points are located where the **vasa recta** (terminal vessels derived from the superior and inferior mesenteric arteries) penetrate through the smooth muscular layer of the colon. As the diverticula enlarge, the vessels are exposed to chronic injury, leading to thinning of the vascular media. Ultimately, the weakened **vessels can ulcerate and rupture**, leading to intraluminal hemorrhage and **painless hematochezia** that is often self-limited but can occasionally result in hemodynamic instability.

Management includes patient resuscitation (eg, intravenous fluids) and colonoscopy, which can diagnose diverticulosis and may identify and treat the source of any active bleeding; angiography or surgery may be required for persistent bleeding.

**(Choice A)** **Angiodysplasias** are abnormal arteriovenous channels that form from ectatic, thin-walled vessels within the gastrointestinal tract. Although they can also cause painless hematochezia, they are identified on colonoscopy as flat, red lesions with a fern-like or arborized appearance.





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Previous



Next



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Notes



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**(Choice A)** **Angiodysplasias** are abnormal arteriovenous channels that form from ectatic, thin-walled vessels within the gastrointestinal tract. Although they can also cause painless hematochezia, they are identified on colonoscopy as flat, red lesions with a fern-like or arborized appearance.

**(Choice B)** Diffuse, continuous mucosal inflammation and erosion extending from the rectum and into the proximal colon are consistent with ulcerative colitis (UC) and typically grossly visible on endoscopy. Although UC also causes hematochezia, it is typically associated with diarrhea, progressive abdominal pain, tenesmus, and fevers.

**(Choice C)** Hemorrhoids are characterized by dilation and tortuosity of the rectal venous plexuses. These appear as a purplish or bluish bulge at the anorectum and are identified easily on physical examination or during colonoscopy.

**(Choice E)** Colorectal adenocarcinoma, which arises typically from **colonic polyps**, can also cause hematochezia due to mucosal sloughing but is usually identified during a colonoscopy as an ulcerated polypoid mass. Patients also often have a history of unexplained weight loss, fatigue, or abnormal stool caliber (eg, pencil-thin stool).

**Educational objective:**

Colonic diverticula form at weak points in the colon wall, typically in areas where the vasa recta penetrate



1



Feedback



Suspend



End Block



pain, tenesmus, and fevers.

**(Choice C)** Hemorrhoids are characterized by dilation and tortuosity of the rectal venous plexuses. These appear as a purplish or bluish bulge at the anorectum and are identified easily on physical examination or during colonoscopy.

**(Choice E)** Colorectal adenocarcinoma, which arises typically from **colonic polyps**, can also cause hematochezia due to mucosal sloughing but is usually identified during a colonoscopy as an ulcerated polypoid mass. Patients also often have a history of unexplained weight loss, fatigue, or abnormal stool caliber (eg, pencil-thin stool).

### Educational objective:

Colonic diverticula form at weak points in the colon wall, typically in areas where the vasa recta penetrate through the smooth muscle. As diverticula enlarge, the vasa recta are exposed and become vulnerable to chronic injury, which can lead to intraluminal hemorrhage and painless hematochezia.

Pathology  
Subject

Gastrointestinal & Nutrition  
System

Diverticular disease  
Topic

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 48-year-old man comes to the emergency department due to 3 days of progressively worsening retrosternal burning chest pain, dysphagia, and odynophagia. His medical problems include hypertension and end-stage renal disease. He underwent cadaveric renal allograft transplantation 8 months ago. The patient's temperature is 38.3 C (101 F), blood pressure is 130/80 mm Hg, and pulse is 94/min. His BMI is 31 kg/m<sup>2</sup>. The oral mucosa is pink and moist without ulcerations. Cardiopulmonary examination is normal. The abdomen is soft with mild epigastric tenderness. The patient's leukocyte count is 4,200/mm<sup>3</sup>. An esophagogastroduodenoscopy demonstrates linear, shallow ulcerations in the lower esophagus. Which of the following is most likely to be seen on esophageal biopsy?

- ☐ A. Enlarged cells with intranuclear inclusions
- ☐ B. Metaplastic columnar epithelium
- ☐ C. Mucosal tear without acute inflammation
- ☐ D. Urease-producing organisms
- ☐ E. Yeast with polysaccharide capsule



1



Feedback



Suspend



End Block



retrosternal burning chest pain, dysphagia, and odynophagia. His medical problems include hypertension and end-stage renal disease. He underwent cadaveric renal allograft transplantation 8 months ago. The patient's temperature is 38.3 C (101 F), blood pressure is 130/80 mm Hg, and pulse is 94/min. His BMI is 31 kg/m<sup>2</sup>. The oral mucosa is pink and moist without ulcerations. Cardiopulmonary examination is normal. The abdomen is soft with mild epigastric tenderness. The patient's leukocyte count is 4,200/mm<sup>3</sup>. An esophagogastroduodenoscopy demonstrates **linear, shallow ulcerations** in the lower esophagus. Which of the following is most likely to be seen on esophageal biopsy?

- ☒ A. Enlarged cells with intranuclear inclusions (74%)
- ☐ B. Metaplastic columnar epithelium (9%)
- ☐ C. Mucosal tear without acute inflammation (8%)
- ☐ D. ~~Urease-producing organisms (3%)~~
- ☐ E. ~~Yeast with polysaccharide capsule (3%)~~

Correct



74%

Answered correctly



01 min, 15 secs

Time spent



11/30/2020

Last updated

Block Time Remaining: 00:26:05

TUTOR

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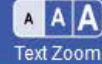
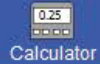
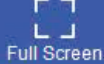
Feedback



Suspend



End Block



This patient's presentation suggests **cytomegalovirus (CMV) esophagitis**, which can occur in immunocompromised patients (eg, HIV, transplant, on immunosuppressant drugs). CMV can be transmitted to **transplant recipients** from the donor organ, or infection can occur subsequently due to chronic immunosuppression. Patients can be asymptomatic or develop a viral prodrome (eg, fever, malaise, myalgias) before organ involvement (eg, esophagitis, pneumonitis, colitis).

CMV esophagitis usually presents with **odynophagia** (pain with swallowing) or **dysphagia** (difficulty swallowing) that can be accompanied by fever or burning chest pain. Endoscopy typically shows **linear and shallow ulcerations** in the lower esophagus that sometimes diffusely involve the esophagus. **Tissue biopsy** usually shows enlarged cells with basophilic or eosinophilic **intranuclear inclusion bodies**.

**(Choice B)** Metaplastic columnar epithelium is seen in **Barrett esophagus**, which is usually due to prolonged gastroesophageal reflux disease (GERD). Histology typically shows tongue-like projections of columnar epithelium with goblet cells (ie, intestinal metaplasia) extending from the distal esophagus to the gastroesophageal junction. The absence of chronic GERD symptoms in this patient makes this less likely.

**(Choice C)** A Mallory-Weiss tear typically presents with hematemesis in association with chest or epigastric pain after repeated retching or vomiting; histology will show a mucosal tear without acute inflammation.







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

columnar epithelium with goblet cells (ie, intestinal metaplasia) extending from the distal esophagus to the gastroesophageal junction. The absence of chronic GERD symptoms in this patient makes this less likely.

**(Choice C)** A Mallory-Weiss tear typically presents with hematemesis in association with chest or epigastric pain after repeated retching or vomiting; histology will show a mucosal tear without acute inflammation.

**(Choice D)** *Helicobacter pylori* is a urease-producing organism that can be associated with gastritis and gastric or duodenal ulcers. It usually does not cause significant esophageal disease.

**(Choice E)** *Cryptococcus neoformans* is a yeast with a polysaccharide capsule. Although disseminated cryptococcosis can occur in immunocompromised patients and involve almost any organ, localized esophageal involvement is more characteristic of *Candida* (a yeast without a polysaccharide capsule).

### Educational objective:

Cytomegalovirus esophagitis can occur in transplant patients and usually presents with odynophagia or dysphagia that can be accompanied by fever or burning chest pain. Endoscopy typically shows linear and shallow ulcerations in the lower esophagus, and histology usually shows enlarged cells with intranuclear inclusions.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 56-year-old man comes to the office for upper abdominal pain occurring with meals for the last month. His symptoms improve when fasting. The patient's other medical problems are coronary artery disease and osteoarthritis. His medications include aspirin, simvastatin, and acetaminophen as needed. The patient drinks 1 or 2 beers daily but does not use tobacco or illicit drugs. Upper endoscopy is performed and reveals a gastric ulcer with a smooth, rounded border and an exudative base. A biopsy of the ulcer is taken and placed into a urea-containing solution that includes phenol red, a pH indicator. Thirty minutes later, the solution has turned pink, indicating a pH increase. This test result suggests that which of the following processes is occurring?

- ☐ A. Clonal proliferation of glandular cells
- ☐ B. Cyclooxygenase inhibition leading to mucosal damage
- ☐ C. Enzymatic production of ammonia
- ☐ D. Gastrin hypersecretion leading to acid overproduction
- ☐ E. Parietal cell destruction due to autoimmune disease



1



Feedback



Suspend



End Block



His symptoms improve when fasting. The patient's other medical problems are coronary artery disease and osteoarthritis. His medications include aspirin, simvastatin, and acetaminophen as needed. The patient drinks 1 or 2 beers daily but does not use tobacco or illicit drugs. Upper endoscopy is performed and reveals a gastric ulcer with a smooth, rounded border and an exudative base. A biopsy of the ulcer is taken and placed into a urea-containing solution that includes phenol red, a pH indicator. Thirty minutes later, the solution has turned pink, indicating a pH increase. This test result suggests that which of the following processes is occurring?

- ☐ A. Clonal proliferation of glandular cells (1%)
- ☐ B. Cyclooxygenase inhibition leading to mucosal damage (6%)
- ☒ C. Enzymatic production of ammonia (83%)
- ☐ D. Gastrin hypersecretion leading to acid overproduction (5%)
- ☐ E. Parietal cell destruction due to autoimmune disease (3%)

Correct



83%



01 min, 10 secs

Time Spent



10/26/2020

Last Updated



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Feedback

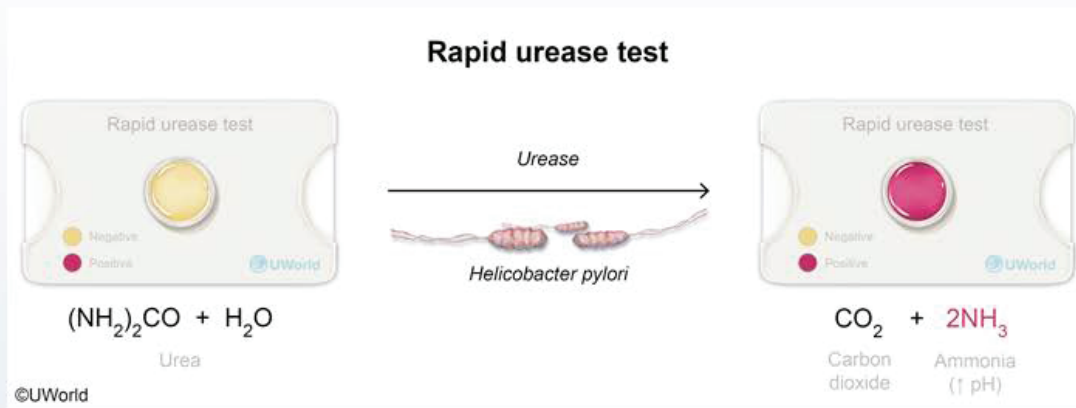


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***Helicobacter pylori*** infection is a common cause of **peptic ulcers**. During endoscopy, biopsy specimens are often obtained for direct tissue diagnosis. In contrast to the time-intensive task of culturing the bacteria, the rapid urease test can be used to quickly diagnose an active infection.

The **rapid urease test** is an indirect test for *H pylori* and relies on the bacterial production of the enzyme **urease**, which splits gastric urea into ammonia and  $\text{CO}_2$ . **Ammonia production** increases the local pH and allows the bacteria to survive in the acidic stomach environment. Biopsy specimens are evaluated in the presence of urea and a pH indicator; evidence of **alkalinization** (due to active ammonia formation) confirms active *H pylori* infection. **Phenol red** is a common reagent that changes from yellow to pink in the



confirms active *H pylori* infection. **Phenol red** is a common reagent that changes from yellow to pink in the presence of an alkaline pH.

**(Choice A)** Gastric adenocarcinoma (ie, clonal proliferation of glandular cells) can present as a gastric ulcer; therefore, gastric ulcers should be biopsied to rule out malignancy. However, malignant ulcers do not cause a color change on urease testing.

**(Choice B)** Nonsteroidal anti-inflammatory drugs (NSAIDs) (eg, aspirin, ibuprofen) are another common cause of peptic ulcers due to their inhibition of the enzyme cyclooxygenase, which is responsible for the synthesis of gastroprotective prostaglandins. However, urease would not be present in an NSAID-induced ulcer.

**(Choice D)** Zollinger-Ellison syndrome is due to gastrin hypersecretion, leading to overproduction of gastric acid and peptic ulcer formation. However, the ulcers would not produce a color change on urease testing.

**(Choice E)** Autoimmune gastritis is due to T-cell mediated destruction of parietal cells. Patients are typically asymptomatic, but prolonged disease leads to pernicious anemia (B12 deficiency due to intrinsic factor destruction) characterized by megaloblastic anemia and neurologic dysfunction. Gastric pH is increased due to loss of parietal cells, but ulcers do not occur in this condition.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

ulcer.

**(Choice D)** Zollinger-Ellison syndrome is due to gastrin hypersecretion, leading to overproduction of gastric acid and peptic ulcer formation. However, the ulcers would not produce a color change on urease testing.

**(Choice E)** Autoimmune gastritis is due to T-cell mediated destruction of parietal cells. Patients are typically asymptomatic, but prolonged disease leads to pernicious anemia (B12 deficiency due to intrinsic factor destruction) characterized by megaloblastic anemia and neurologic dysfunction. Gastric pH is increased due to loss of parietal cells, but ulcers do not occur in this condition.

### Educational objective:

*Helicobacter pylori* produces the enzyme urease, which splits urea into  $\text{CO}_2$  and ammonia and neutralizes the local acidic gastric pH. Active infection can be confirmed through rapid urease testing, in which gastric mucosa is evaluated in the presence of urea and a pH indicator. Evidence of alkalization (due to ammonia formation) is confirmatory.

### References

- [Diagnosis of Helicobacter pylori using the rapid urease test.](#)



1



Feedback



Suspend



End Block





A 79-year-old woman comes to the office for evaluation of difficulty walking due to fatigue and bilateral leg pain. The pain started in her lower legs 3 weeks ago and progressed to involve the muscles of her thighs also. In addition, she has noted red spots on her legs. The patient has lived alone since her husband died 3 years ago and is largely homebound. Her diet consists mostly of bread and canned meat products. On examination, the gums are swollen and tender. The patient's skin findings are shown in the [exhibit](#). Muscles of the lower limbs are tender to palpation. Imaging studies reveal a tibial subperiosteal hematoma. Which of the following nutrient deficiencies is most likely responsible for this patient's symptoms?

- ☐ A. Ascorbic acid
- ☐ B. Biotin
- ☐ C. Folic acid
- ☐ D. Linoleic acid
- ☐ E. Pyridoxine
- ☐ F. Riboflavin



Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



muscles of the lower limbs are tender to palpation. Imaging studies reveal a tibial subperiosteal hematoma. Which of the following nutrient deficiencies is most likely responsible for this patient's symptoms?

- ☐ A. Ascorbic acid
- ☐ B. Biotin
- ☐ C. Folic acid
- ☐ D. Linoleic acid
- ☐ E. Pyridoxine
- ☐ F. Riboflavin
- ☐ G. Thiamine
- ☐ H. Vitamin K
- ☐ I. Zinc

**Submit**

Block Time Remaining: 00:27:26

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

hematoma. Which of the following nutrient deficiencies is most likely responsible for this patient's symptoms?

- ✓ ☒ A. Ascorbic acid (77%)
- ☐ B. Biotin (0%)
- ☐ C. Folic acid (2%)
- ☐ D. Linoleic acid (0%)
- ☐ E. Pyridoxine (1%)
- ☐ F. Riboflavin (1%)
- ☐ G. Thiamine (1%)
- ☐ H. Vitamin K (12%)
- ☐ I. Zinc (1%)

Correct

77%

Answered correctly



56 secs

Time Spent



01/10/2021

Last Updated

Block Time Remaining: 00:28:11

<https://t.me/USMLEWorldStep1>

0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient with perifollicular hemorrhages, myalgias, subperiosteal hematoma, and **gingivitis** has typical features of **scurvy**. Scurvy, which is due to a deficiency of **ascorbic acid** (vitamin C), is uncommon in developed countries as this vitamin is widely available in fruits, vegetables, and a variety of other foods. However, it may occasionally be seen in patients with abnormal eating patterns, including the elderly, alcoholics, and persons who live alone. Other possible signs of scurvy include hemarthrosis, **petechial hemorrhages**, impaired wound healing, and weakened immune responses to local infections.

Ascorbic acid is a cofactor in a number of reactions but is especially important in the hydroxylation of proline and lysine residues. In particular, synthesis of **collagen** requires extensive formation of **hydroxyproline** in the procollagen polypeptide, and ascorbic acid deficiency leads to reduced production of collagen with lower tensile strength. Collagen defects in blood vessel walls lead to widespread microvascular bleeding.

**(Choice B)** Biotin plays a role in a number of carboxylation reactions. Deficiency is rare but can present with rash, hair loss, and neuropsychiatric defects.

**(Choice C)** Folic acid deficiency is characterized by megaloblastic anemia and fetal neural tube defects.

**(Choice D)** Linoleic acid is an essential fatty acid used in the synthesis of arachidonic acid. Deficiency is not well characterized, but reported features include growth deficiency and neurovisual defects.



Feedback



Suspend



End Block

Exhibit Display



Zoom In Zoom Out Reset New | Existing My Notebook

not well characterized, but reported features include growth deficiency and neurovisual defects

Block Time Remaining: 00:28:11

<https://t.me/USMLEWorldStep1>







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice B)** Biotin plays a role in a number of carboxylation reactions. Deficiency is rare but can present with rash, hair loss, and neuropsychiatric defects.

**(Choice C)** Folic acid deficiency is characterized by megaloblastic anemia and fetal neural tube defects.

**(Choice D)** Linoleic acid is an essential fatty acid used in the synthesis of arachidonic acid. Deficiency is not well characterized, but reported features include growth deficiency and neurovisual defects.

**(Choice E)** Pyridoxine (vitamin B<sub>6</sub>) deficiency is characterized by cheilosis, glossitis, dermatitis, and peripheral neuropathy.

**(Choice F)** Vitamin B<sub>2</sub> (riboflavin) deficiency is characterized by angular stomatitis, cheilitis, glossitis, seborrheic dermatitis, eye changes (eg, keratitis, corneal neovascularization), and anemia.

**(Choice G)** Vitamin B<sub>1</sub> (thiamine) deficiency causes beriberi (peripheral neuropathy, muscle wasting, and heart failure), Wernicke syndrome (nystagmus, ataxia, and ophthalmoplegia), and Korsakoff psychosis.

**(Choice H)** Vitamin K deficiency is characterized by a bleeding diathesis (but not painful gums).

**(Choice I)** Zinc deficiency is characterized by acrodermatitis enteropathica, growth retardation, and infertility.

**Educational objective:**

Block Time Remaining: 00:28:11

<https://t.me/USMLEWorldStep1>



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

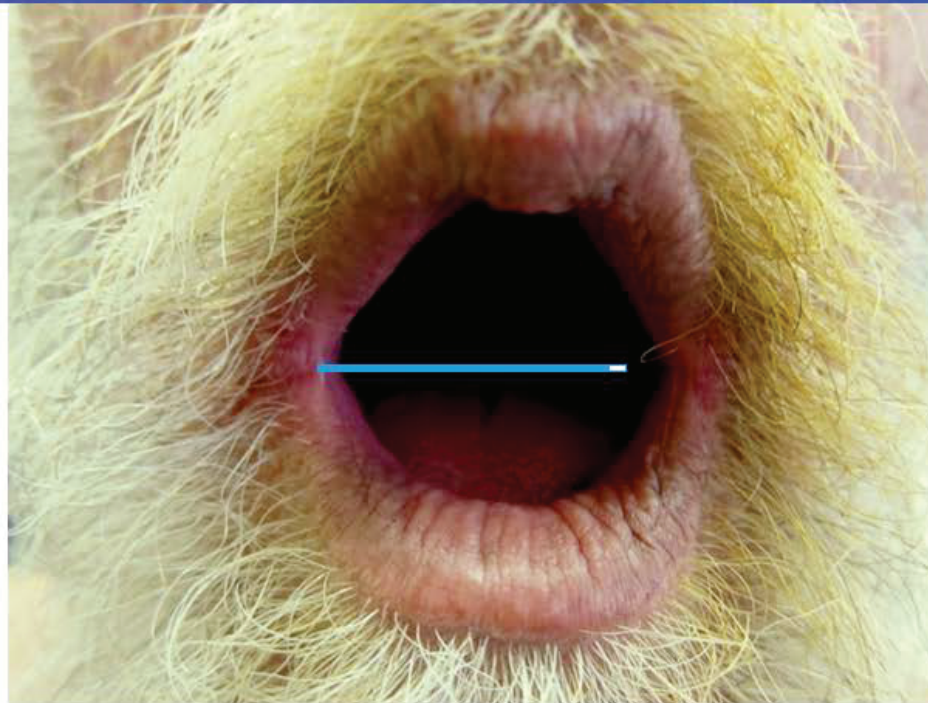
Reverse Color

Text Zoom

Settings

(Choice B) Biotin plays a role in a number of carboxylation reactions. Deficiency is rare but can present

## Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Educational Objective:

Block Time Remaining: 00:28:11

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



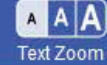
Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice F)** Vitamin B<sub>2</sub> (riboflavin) deficiency is characterized by angular stomatitis, cheilitis, glossitis, seborrheic dermatitis, eye changes (eg, keratitis, corneal neovascularization), and anemia.

**(Choice G)** Vitamin B<sub>1</sub> (thiamine) deficiency causes beriberi (peripheral neuropathy, muscle wasting, and heart failure), Wernicke syndrome (nystagmus, ataxia, and ophthalmoplegia), and Korsakoff psychosis.

**(Choice H)** Vitamin K deficiency is characterized by a bleeding diathesis (but not painful gums).

**(Choice I)** Zinc deficiency is characterized by acrodermatitis enteropathica, growth retardation, and infertility.

### Educational objective:

Ascorbic acid (vitamin C) is a cofactor in the hydroxylation of proline and lysine residues and is important in the synthesis of collagen. Deficiency (scurvy) is characterized by microvascular bleeding, gingivitis, and impaired wound healing.

Biochemistry

Subject

Gastrointestinal &amp; Nutrition

System

Vitamin C deficiency

Topic

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Block Time Remaining: 00:28:11

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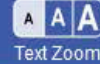
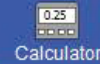
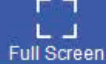


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A 54-year-old man is evaluated for episodic abdominal discomfort, bloating sensation, flatulence, and occasional diarrhea. He has no blood in the stool or weight loss. The patient has tried avoiding dairy products, but the symptoms did not improve. On examination, there is mild epigastric tenderness on deep palpation. Stool occult blood testing is positive. Histopathological evaluation of hyperemic mucosa seen during gastrointestinal endoscopy reveals hyperplasia of branched, tubular submucosal glands containing alkaline secretions. Which of the following areas is the most likely site of biopsy in this patient?

- ☐ A. Antrum of the stomach
- ☐ B. First part of the duodenum
- ☐ C. Fundus of the stomach
- ☐ D. Mid-part of the jejunum
- ☐ E. Terminal ileum
- ☐ F. Transverse colon

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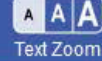
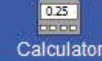
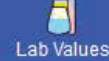
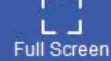
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Feedback

Suspend

End Block



A 54-year-old man is evaluated for episodic abdominal discomfort, bloating sensation, flatulence, and occasional diarrhea. He has no blood in the stool or weight loss. The patient has tried avoiding dairy products, but the symptoms did not improve. On examination, there is mild epigastric tenderness on deep palpation. Stool **occult blood** testing is positive. Histopathological evaluation of hyperemic mucosa seen during gastrointestinal endoscopy reveals **hyperplasia** of branched, tubular submucosal glands containing alkaline secretions. Which of the following areas is the most likely site of biopsy in this patient?

- ☐ A. Antrum of the stomach (6%)
- ☒ B. First part of the duodenum (77%)
- ☐ C. Fundus of the stomach (3%)
- ☐ D. Mid-part of the jejunum (5%)
- ☐ E. Terminal ileum (4%)
- ☐ F. Transverse colon (3%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The integrity of the small intestinal mucosa depends on the complete and rapid neutralization of hydrochloric acid in gastric contents. This is accomplished by alkaline secretions from 2 primary sources:

- **Submucosal (Brunner) glands** secrete copious amounts of alkaline mucus into the duodenum. These glands are most numerous at the pylorus but may be found intermittently up to the ampulla of Vater. The ducts of these glands pass through the muscularis mucosa and terminate in the mucosal crypts (crypts of Lieberkühn).
- The epithelial cells of the pancreatic ductules and ducts produce watery secretions containing high concentrations of bicarbonate ions. The strongly alkaline pancreatic secretions are then emptied into the duodenum at the ampulla.

Tactile stimulation of the duodenal mucosa and increased parasympathetic activity following meals induce bicarbonate secretion from the submucosal glands. In addition, the presence of acid in the duodenum and jejunum causes release of **secretin** from the mucosa, stimulating secretion of bicarbonate from the submucosal glands and pancreas. Excess gastric acid secretion, such as seen in *Helicobacter pylori* infection, can cause increased production of secretin that, over time, can lead to hyperplasia of the submucosal glands.



0



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

infection, can cause increased production of secretin that, over time, can lead to hyperplasia of the submucosal glands.

**(Choices A and C)** The antrum of the stomach contains numerous pyloric glands that secrete copious mucus for protection of the mucosa. Gastric acid is primarily secreted by parietal cells of the oxyntic glands at the body and fundus of the stomach.

**(Choice D)** The mucosal crypts in the jejunum contain goblet cells (secrete mucus) and enterocytes (secrete water and electrolytes). These secretions have only minimal bicarbonate content.

**(Choices E and F)** Bicarbonate is secreted by epithelial cells in the ileum and colon to neutralize acid produced by colonic bacteria. However, this bicarbonate is secreted at the villi in the ileum and crypts in the colon, and submucosal glands are not present in these locations.

### Educational objective:

Gastric acid is neutralized by bicarbonate from the submucosal glands of the duodenum (Brunner glands) and from pancreatic duct secretions. Chronic overproduction of gastric acid can lead to hyperplasia of the submucosal glands.

Anatomy

Gastrointestinal &amp; Nutrition

H pylori

Subject

System

Topic

Block Time Remaining: 00:29:18

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 3-week-old male born to a 23-year-old Caucasian primigravida develops projectile non-bilious vomiting after every meal. Abdominal inspection reveals prominent peristalsis in the epigastrium and an olive-sized mass is felt on deep palpation of the right upper abdomen. The mass most likely represents:

- ☐ A. Infection focus
- ☐ B. Neoplastic cell proliferation
- ☐ C. Smooth muscle hypertrophy
- ☐ D. Pancreatic juice accumulation
- ☐ E. Biliary duct distension

**Submit**

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 3-week-old male born to a 23-year-old Caucasian primigravida develops projectile non-bilious vomiting after every meal. Abdominal inspection reveals prominent peristalsis in the epigastrium and an olive-sized mass is felt on deep palpation of the right upper abdomen. The mass most likely represents:

- ☐ A. Infection focus (1%)
- ☐ B. Neoplastic cell proliferation (1%)
- ☒ C. Smooth muscle hypertrophy (85%)
- ☐ D. Pancreatic juice accumulation (1%)
- ☐ E. Biliary duct distension (9%)

**Correct** 85%  
Answered correctly 22 secs  
Time Spent 11/22/2020  
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Explanation

Block Time Remaining: 00:29:40

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Feedback



Suspend



End Block





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Congenital pyloric stenosis is a relatively common disorder that is encountered primarily in male infants (at a 3:1 ratio) and characterized by a multifactorial pattern of inheritance. Infants typically present with recurrent projectile nonbilious vomiting, and physical examination demonstrates visible peristalsis and the presence of an olive-sized mass in the distal stomach or pyloric region. The mass is thought to develop secondary to hypertrophy of the pyloric muscularis mucosae. The narrowing of the pyloric channel is thought to be exacerbated by localized edema and inflammation. The stenosis is relieved by surgical splitting of the muscle.

**(Choices A, D, and E)** Infection, pancreatic juice accumulation, and biliary duct distension are not associated with pyloric stenosis.

**(Choice B)** Acquired pyloric stenosis occurs in adults and is associated with gastritis, peptic ulcers in the pylorus, or a neoplastic process (eg, carcinoma of the pyloric region or lymphoma). Neoplasm in this area would not be expected in an infant, however.

**Educational Objective:**

Congenital pyloric stenosis arises secondary to hypertrophy of the pyloric muscularis mucosae.



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Feedback



Suspend



End Block



A 60-year-old man is found to have a 5-cm exophytic mass in the ascending colon during a screening colonoscopy. Biopsy of the mass shows adenocarcinoma. The patient has no personal or family history of malignancy or colonic polyps. His medical problems include hypertension, and he does not use tobacco or alcohol. CT scan of the chest and abdomen reveals no metastatic lesions in the lungs or liver. A right colectomy is performed. The presence of which of the following indicates a poor prognosis in this patient?

- ☐ A. Abundant, well-formed glands in the tumor
- ☐ B. Cytokeratin expression by the malignant cells
- ☐ C. Malignant cells invading the lamina propria
- ☐ D. Prominent lymphocyte infiltration of the tumor
- ☐ E. Tumor cell deposits in the regional lymph nodes

**Submit**



A 60-year-old man is found to have a 5-cm exophytic mass in the ascending colon during a screening colonoscopy. Biopsy of the mass shows adenocarcinoma. The patient has no personal or family history of malignancy or colonic polyps. His medical problems include hypertension, and he does not use tobacco or alcohol. CT scan of the chest and abdomen reveals no metastatic lesions in the lungs or liver. A right colectomy is performed. The presence of which of the following indicates a poor prognosis in this patient?

- ☐ A. Abundant, well formed glands in the tumor (0%)
- ☐ B. Cytokeratin expression by the malignant cells (1%)
- ☐ C. Malignant cells invading the lamina propria (22%)
- ☐ D. Prominent lymphocyte infiltration of the tumor (0%)
- ☒ E. Tumor cell deposits in the regional lymph nodes (74%)

Correct

 74%  
Answered correctly 01 min, 05 secs  
Time Spent 09/05/2020  
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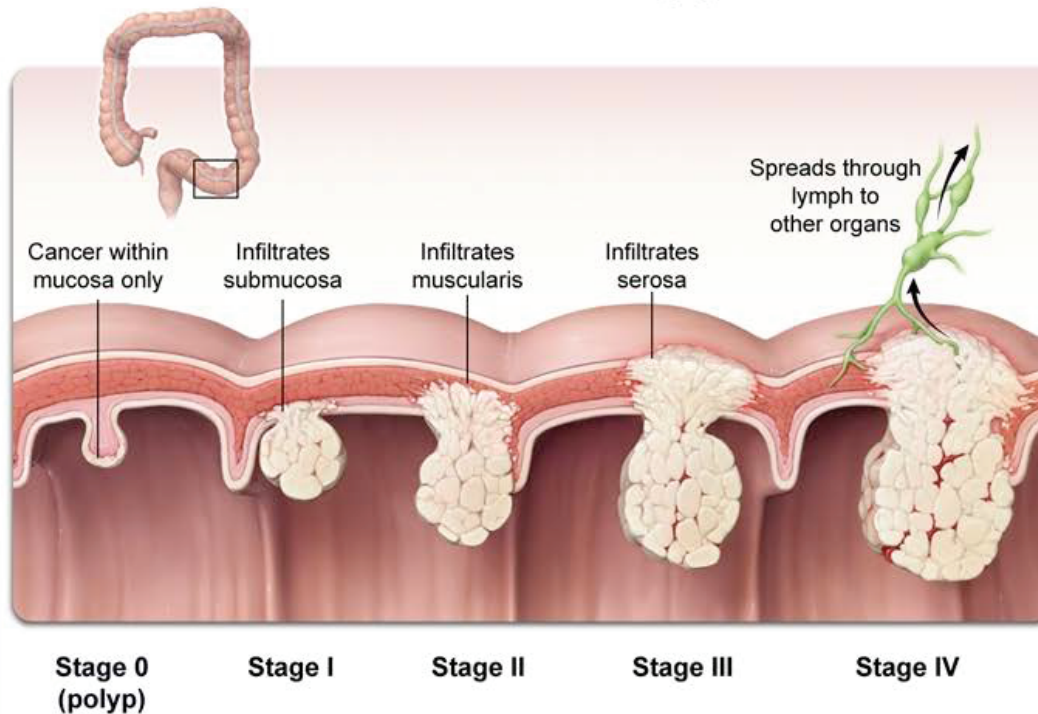
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End Block



## Colorectal cancer staging



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Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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The **prognosis of colorectal cancer** is most tightly correlated with tumor stage at diagnosis. Stage reflects the **degree of tumor invasion and spread** from the initial site of formation. Colorectal tumors confined to the basement membrane or lamina propria are considered to be carcinoma in situ and have an excellent 5-year survival rate (>90%). Invasion of the tumor into the muscularis propria, the location of the colonic lymphatic channels, is associated with a slightly worse prognosis (5-year survival rate of 70%-80%) due to elevated rates of tumor spread through lymphatics or to adjacent organs.

The prognosis of colon cancer deteriorates when tumor cells are identified in regional lymph nodes (5-year survival rate of 50%-80%). **Lymph node spread** is thought to be one of the strongest predictors of metastatic potential and, therefore, indicates an **increased risk** for incurable, distant disease. Metastatic spread to distant organs (eg, lungs, liver) is associated with the worst 5-year survival rates (<15%).

**(Choice A)** Tumor grade, the degree of cellular differentiation of tumor cells, also affects prognosis. Well-differentiated (low-grade) colonic tumors have glandular structure and are associated with a better prognosis than poorly differentiated (high-grade) colonic tumors, which appear as sheets or cords of cells with pleomorphism, high mitotic rates, and other signs of significant cellular aberration. Grade is a less important prognostic indicator than stage.



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

with pleomorphism, high mitotic rates, and other signs of significant cellular aberration. Grade is a less important prognostic indicator than stage.

**(Choice B)** Cytokeratin 20 is a marker of intestinal cell differentiation. Testing for the presence of this structural protein helps confirm that adenocarcinomas are of intestinal origin; it is not a prognostic indicator.

**(Choice C)** The invasion of colorectal cancer into the lamina propria is considered to be carcinoma in situ because lymphatic channels do not arise until the subsequent layer (muscularis propria). Patients with colorectal tumors confined to the basement membrane or lamina propria have an excellent prognosis.

**(Choice D)** Cytotoxic T-cell (lymphocytic) invasion of tumor cells is a favorable prognostic indicator as it signifies immune recognition. It is associated with a lower risk of metastases and improved survival.

**Educational objective:**

Tumor stage (degree of invasion/spread) is the most important prognostic determinant for colorectal cancer. Tumors confined to the basement membrane and lamina propria are early stage and have the best prognosis. Outcomes generally deteriorate as the stage advances: spread of tumor into the muscularis propria → regional lymph nodes → distant sites.

Pathology

Gastrointestinal &amp; Nutrition

Colorectal polyps and cancer

Block Time Remaining: 00:30:45

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 15-month-old boy is brought to the office by his parents for poor weight gain. The parents have also noticed frequent, large, foul-smelling stools. He was admitted to the hospital for a prolonged bout of bacterial pneumonia 6 months ago. Both parents are healthy and have no similar symptoms. The child was born at term at home. He is at the 20th percentile for length and 3rd percentile for weight. Vital signs are normal. On examination, the child appears thin and has a nontender, nondistended abdomen. Which of the following is most likely present in this patient?

- ☐ A. Decreased fecal calcium content
- ☐ B. Decreased fecal elastase
- ☐ C. Increased fecal calprotectin
- ☐ D. Increased fecal chymotrypsin
- ☐ E. Increased pancreatic bicarbonate secretion

**Submit**

Block Time Remaining: 00:30:46

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Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Settings

A 15-month-old boy is brought to the office by his parents for poor weight gain. The parents have also noticed frequent, large, foul-smelling stools. He was admitted to the hospital for a prolonged bout of bacterial pneumonia 6 months ago. Both parents are healthy and have no similar symptoms. The child was born at term at home. He is at the 20th percentile for length and 3rd percentile for weight. Vital signs are normal. On examination, the child appears thin and has a nontender, nondistended abdomen. Which of the following is most likely present in this patient?

- ☐ A. Decreased fecal calcium content (4%)
- ☒ B. Decreased fecal elastase (67%)
- ☐ C. Increased fecal calprotectin (4%)
- ☐ D. Increased fecal chymotrypsin (14%)
- ☐ E. Increased pancreatic bicarbonate secretion (9%)

Correct

 67%  
Answered correctly 38 secs  
Time Spent 12/08/2020  
Last Updated

Block Time Remaining: 00:31:23

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Feedback



Suspend



End Block

## Features of cystic fibrosis

### Pathogenesis

- Autosomal recessive mutation ( $\Delta F508$ ) impairs CFTR function
- Decreased water content causes **thick, viscous mucus**:
  - Chronic airway obstruction
  - Gastrointestinal malabsorption

### Clinical manifestations

- Chronic, productive cough
- Recurrent **sinopulmonary infections** (eg, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, & *Burkholderia cepacia* complex)
- **Pancreatic insufficiency**
- Male infertility (bilateral absence of vas deferens)
- Elevated sweat chloride levels



## Diagnosis

- Elevated sweat chloride levels
- Nasal potential difference measurements
- Genetic testing for *CFTR* mutations

**CFTR** = cystic fibrosis transmembrane conductance regulator.

This patient with failure to thrive, steatorrhea, and a hospitalization for pneumonia most likely has **cystic fibrosis** (CF). CF is an autosomal recessive disorder in which a defective **chloride channel** causes the accumulation of thick, dehydrated secretions in **multiple organs**.

In the **pancreas**, viscous mucus obstructs small ducts and acini, preventing **digestive enzymes** from reaching the intestinal lumen and leading to progressive pancreatic inflammation and fibrosis. This ultimately causes **pancreatic insufficiency**, which may be present at birth in patients with CF and typically progresses throughout childhood. Signs of fat and protein malabsorption due to pancreatic insufficiency include **steatorrhea** (bulky, foul-smelling stools), **failure to thrive**, and fat-soluble vitamin deficiencies (A, D, E, and K).

**Elastase** is a pro-enzyme (ie, zymogen) produced by pancreatic acinar cells and activated by trypsin within the duodenal lumen. Because elastase production and secretion are decreased in patients with pancreatic

deficiencies (A, D, E, and K).

**Elastase** is a pro-enzyme (ie, zymogen) produced by pancreatic acinar cells and activated by trypsin within the duodenal lumen. Because elastase production and secretion are decreased in patients with pancreatic insufficiency, fecal elastase levels are also decreased; the presence of **low fecal elastase** is an accurate and noninvasive method for diagnosing pancreatic insufficiency of any cause (eg, CF, chronic pancreatitis).

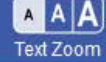
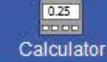
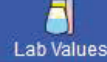
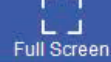
**(Choice A)** Dietary absorption of calcium is decreased in CF in part due to vitamin D deficiency, which leads to both hypocalcemia and increased calcium fecal concentration.

**(Choice C)** Calprotectin is a protein derived from neutrophils that is released into the stool of patients with inflammatory diarrhea (eg, ulcerative colitis, Crohn disease). Fecal calprotectin levels are not increased in CF.

**(Choice D)** Like elastase, chymotrypsin is a pancreatic digestive enzyme whose fecal concentration would be decreased (not increased) in patients with pancreatic insufficiency.

**(Choice E)** Bicarbonate is produced and secreted by the pancreas to neutralize gastric acid and raise duodenal pH. Because patients with pancreatic insufficiency have less bicarbonate secretion, duodenal pH will decrease. The low pH can inactivate digestive enzymes produced by the stomach and intestine, further impairing nutrient absorption.





leads to both hypocalcemia and increased calcium fecal concentration.

**(Choice C)** Calprotectin is a protein derived from neutrophils that is released into the stool of patients with inflammatory diarrhea (eg, ulcerative colitis, Crohn disease). Fecal calprotectin levels are not increased in CF.

**(Choice D)** Like elastase, chymotrypsin is a pancreatic digestive enzyme whose fecal concentration would be decreased (not increased) in patients with pancreatic insufficiency.

**(Choice E)** Bicarbonate is produced and secreted by the pancreas to neutralize gastric acid and raise duodenal pH. Because patients with pancreatic insufficiency have less bicarbonate secretion, duodenal pH will decrease. The low pH can inactivate digestive enzymes produced by the stomach and intestine, further impairing nutrient absorption.

### Educational objective:

Pancreatic insufficiency is common in cystic fibrosis because thick, viscous secretions in the pancreas block digestive enzymes, leading to malabsorption (eg, steatorrhea, failure to thrive). The presence of low fecal elastase is an accurate and noninvasive method for diagnosing pancreatic insufficiency.

### References

- [Pancreatic pathophysiology in cystic fibrosis](#)

Block Time Remaining: 00:31:23

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 44-year-old woman comes to the clinic after several "near collisions" over the past month while driving at night. She also has generalized pruritus. The patient has not seen a physician for several years and has missed several scheduled appointments. She takes no medications. On physical examination, her skin is diffusely coarse and dry. Which of the following processes is most likely responsible for these findings?

- ☐ A. Chronic renal failure
- ☐ B. Hemolytic anemia
- ☐ C. Inadequate sunlight exposure
- ☐ D. Prolonged biliary obstruction
- ☐ E. Rheumatoid arthritis
- ☐ F. Strict vegan diet

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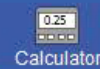
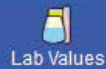
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A 44-year-old woman comes to the clinic after several "near collisions" over the past month while driving at night. She also has generalized pruritus. The patient has not seen a physician for several years and has missed several scheduled appointments. She takes no medications. On physical examination, her skin is diffusely coarse and dry. Which of the following processes is most likely responsible for these findings?

- ☐ A. Chronic renal failure (3%)
- ☐ B. Hemolytic anemia (3%)
- ☐ C. Inadequate sunlight exposure (2%)
- ☒ D. Prolonged biliary obstruction (64%)
- ☐ E. Rheumatoid arthritis (1%)
- ☐ F. Strict vegan diet (23%)

Correct

64%  
Answered correctly

01 min, 04 secs  
Time Spent

01/10/2021  
Last Updated

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Vitamin A deficiency	
<b>Causes</b>	<ul style="list-style-type: none"><li>• Insufficient dietary intake</li><li>• Pancreatic insufficiency (chronic pancreatitis, cystic fibrosis)</li><li>• Cholestatic liver disease/biliary obstruction</li><li>• Intestinal malabsorption (inflammatory bowel disease, bariatric surgery)</li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• <b>Night blindness</b></li><li>• Severe eye dryness &amp; <b>corneal ulceration</b></li><li>• Hyperkeratosis</li><li>• Growth retardation</li></ul>

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This patient's impaired driving in low light conditions ("night blindness") and thickened, dry skin (hyperkeratosis) are suggestive of **vitamin A deficiency**. Dietary intake of vitamin A comes from a combination of beta-carotene, a provitamin found in plants, and preformed vitamin A from animal sources.

Vitamin A is necessary for **vision** (phototransduction, retinal and conjunctival development) and





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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This patient's impaired driving in low light conditions ("night blindness") and thickened, dry skin (hyperkeratosis) are suggestive of **vitamin A deficiency**. Dietary intake of vitamin A comes from a combination of beta-carotene, a provitamin found in plants, and preformed vitamin A from animal sources. Vitamin A is necessary for **vision** (phototransduction, retinal and conjunctival development) and **keratinocyte differentiation**. Most individuals in the United States have adequate dietary intake of vitamin A, but patients may develop deficiency due to malabsorption related to biliary obstruction, exocrine pancreatic insufficiency, or small-bowel resection (eg, Crohn disease, bariatric surgery).

This patient, a middle-aged woman with generalized pruritus and signs of vitamin A deficiency, likely has underlying **primary biliary cholangitis** (PBC), a common autoimmune disease characterized by destruction of small bile ducts in the liver. Bile acids are important for solubilization and absorption of fats; patients with chronic biliary obstruction due to PBC may develop **malabsorption** of fats and **fat-soluble vitamins** (A, D, E, and K). Patients with PBC frequently have generalized pruritus due to bile acid accumulation in the skin. Visible jaundice is often not apparent until later in the disease course.

**(Choices A and C)** Inadequate exposure to sunlight can cause vitamin D deficiency in individuals without adequate dietary vitamin D intake. Chronic renal failure can also result in vitamin D deficiency due to reduced production of 1,25-dihydroxyvitamin D.

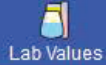
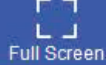
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Feedback

Suspend

End Block



**(Choices A and C)** Inadequate exposure to sunlight can cause vitamin D deficiency in individuals without adequate dietary vitamin D intake. Chronic renal failure can also result in vitamin D deficiency due to reduced production of 1,25-dihydroxyvitamin D.

**(Choice B)** Sickle cell disease is a form of chronic hemolytic anemia that can cause retinopathy due to microvascular occlusion, retinal ischemia, and neovascularization/hemorrhage. However, vision impairment would not be restricted to nighttime, and affected patients would likely have other vasoocclusive symptoms.

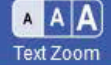
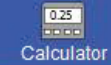
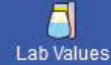
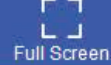
**(Choice E)** Rheumatoid arthritis can cause [episcleritis](#) or [scleritis](#), which usually presents with ocular discomfort rather than night blindness.

**(Choice F)** A strict vegan diet can cause cobalamin, but not vitamin A, deficiency. Dietary deficiency of vitamin A is rarely seen in the United States and usually occurs in patients with highly unusual dietary patterns, severe mental illness, or alcoholism.

**Educational objective:**

Vitamin A deficiency causes night blindness and hyperkeratosis. Deficiency of this fat-soluble vitamin can develop in patients with biliary disorders, exocrine pancreatic insufficiency, or intestinal malabsorption.





A 5-year-old boy is brought to the emergency department due to diarrhea and a low-grade fever. He attends a day care center where other children developed similar symptoms. The boy has no known medical problems. He is up to date with age-appropriate vaccinations. He has not traveled abroad. Physical examination shows abdominal tenderness on deep palpation but no rigidity. Stool is sent for culture, and the patient is diagnosed with *Shigella sonnei* infection. The outbreak is reported to public health authorities and is traced to consumption of a potato salad handled by a food worker who recently had a mild diarrheal illness. Which of the following cells are primarily responsible for uptake of the bacteria that initiated the infection in this boy?

- ☐ A. Endothelial cells
- ☐ B. Enteroendocrine cells
- ☐ C. Goblet cells
- ☐ D. Microfold (M) cells
- ☐ E. Paneth cells
- ☐ F. Polymorphonuclear cells







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

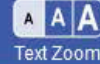
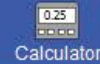
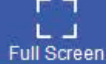
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attends a day care center where other children developed similar symptoms. The boy has no known medical problems. He is up to date with age-appropriate vaccinations. He has not traveled abroad. Physical examination shows abdominal tenderness on deep palpation but no rigidity. Stool is sent for culture, and the patient is diagnosed with *Shigella sonnei* infection. The outbreak is reported to public health authorities and is traced to consumption of a potato salad handled by a food worker who recently had a mild diarrheal illness. Which of the following cells are primarily responsible for uptake of the bacteria that initiated the infection in this boy?

- ☐ A. Endothelial cells (11%)
- ☐ B. Enteroendocrine cells (4%)
- ☐ C. Goblet cells (3%)
- ☒ D. Microfold (M) cells (65%)
- ☐ E. Paneth cells (7%)
- ☐ F. Polymorphonuclear cells (6%)





**Shigellosis** is an infectious form of hemorrhagic diarrhea that can be caused by a variety of *Shigella* species (*S dysenteriae*, *S flexneri*, *S boydii*, *S sonnei*); shigellosis is most commonly due to *S sonnei* in industrialized nations (80%).

*Shigella* cannot bind all intestinal cells. *Shigella* exhibits specificity for the **microfold (M) cells** at the base of mucosal villi within a **Peyer patch** region of the ileal mucosa. M cells sample gut lumen contents and transfer antigens to their basal lamina within endosomes. At the base of the cell, macrophages and lymphocytes ready to mount an immune response await within a special pocket (microfold).

*Shigella* penetrates the mucous membrane by passing through M cells via **endocytosis**. It subsequently lyses the endosome, multiplies, and spreads laterally into other epithelial cells. This results in denuding and ulceration of the mucosa and subsequent leakage of blood, inflammatory elements, and mucus into the intestinal lumen. Patients pass frequent stools mixed with **blood and mucus**. Stools are frequent and loose due to water absorption inhibition.

**(Choice A)** Endothelial cells form the innermost lining of blood vessels. The Shiga-like toxin of *Escherichia coli* O157:H7 can cause toxicity to renal endothelial cells, leading to renal insufficiency and uremia.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



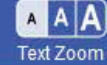
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Settings

uremia.

**(Choice B)** Enteroendocrine cells in the gastrointestinal tract secrete hormones such as somatostatin and cholecystokinin.

**(Choice C)** Goblet cells are responsible for mucus secretion into the gut lumen. Mucus release is increased in inflammatory states; stool will have visible mucus in conditions such as inflammatory diarrhea, giardiasis, and Crohn disease.

**(Choice E)** Paneth cells, which occur in small groups at the base of intestinal crypts, are both phagocytic and secretory, thereby providing first-line immune defense against microorganisms. They secrete lysozyme (an enzyme that dissolves the cell walls of many bacteria) and defensins (polypeptides with antimicrobial properties).

**(Choice F)** In patients with diarrhea, stool is tested for fecal leukocytes (polymorphonuclear cells) when it is unclear whether the etiology is noninflammatory (enterotoxigenic *E coli*, enteroaggregative *E coli*, *Vibrio cholerae*, *Clostridium perfringens*, *Rotavirus*) or inflammatory (*Shigella*, enterohemorrhagic *E coli*, enteroinvasive *E coli*, *Clostridium difficile*, *Campylobacter jejuni*).

### Educational objective:

Shigellosis is an infectious disease that can be caused by variety of *Shigella* species; *S sonnei* is the most



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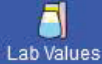


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increased in inflammatory states; stool will have visible mucus in conditions such as inflammatory diarrhea, giardiasis, and Crohn disease.

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### Educational objective:

Shigellosis is an infectious disease that can be caused by variety of *Shigella* species; *S sonnei* is the most common cause of shigellosis in industrialized nations. *Shigella* invades the gastrointestinal mucosa by gaining access to microfold cells in ileal Peyer patches through endocytosis. *Shigella* subsequently lyses the endosome and spreads laterally into other epithelial cells, causing cell death and ulceration with hemorrhage and diarrhea.

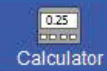
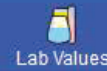




Researchers studying neural crest cell migration in a human fetus observe normal activity beginning at the 8th week of embryogenesis with interruption during the 12th week, when migration is typically completed. Which of the following structures is most likely to lack innervation as a result of this disruption?

- ☐ A. Esophagus
- ☐ B. Duodenum
- ☐ C. Jejunum
- ☐ D. Ileum
- ☐ E. Cecum
- ☐ F. Transverse colon
- ☐ G. Rectum

**Submit**



Researchers studying neural crest cell migration in a human fetus observe normal activity beginning at the 8th week of embryogenesis with interruption during the 12th week, when migration is typically completed. Which of the following structures is most likely to lack innervation as a result of this disruption?

- ☐ A. Esophagus (6%)
- ☐ B. Duodenum (3%)
- ☐ C. Jejunum (1%)
- ☐ D. Ileum (3%)
- ☐ E. Cecum (5%)
- ☐ F. Transverse colon (10%)
- ☒ G. Rectum (68%)

Correct

68%  
Answered correctly

26 secs  
Time Spent

10/01/2020  
Last Updated

Block Time Remaining: 00:33:04

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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## Hirschsprung disease

### Pathophysiology

- Failure of neural crest cell migration caudally to distal colon
- Absent parasympathetic ganglia in affected submucosal & myenteric plexus
- Chronically contracted colonic segment

### Clinical features

- Delayed passage of meconium in neonates
- Chronic constipation
- Abdominal distension

### Evaluation

- Contrast enema: narrow rectosigmoid area with dilated proximal colon
- Rectal suction biopsy (diagnostic): absent submucosal ganglia

Normally, **neural crest cells** start migrating to the intestinal wall in early embryogenesis and give rise to **ganglion cells** of the submucosal (Meissner) and myenteric (Auerbach) plexus of the bowel wall. These parasympathetic ganglia are responsible for intestinal peristalsis. Neural crest cells enter the developing foregut mesenchyme and then **migrate caudally** along the entire length of the bowel; they are present in the wall of proximal colon by the 8th week of gestation and in the rectum by the 12th week.

The **arrest of migration** of neural crest cells causes **Hirschsprung disease**, in which a distal segment of



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the wall of proximal colon by the 8th week of gestation and in the rectum by the 12th week.

The **arrest of migration** of neural crest cells causes **Hirschsprung disease**, in which a distal segment of colon **lacks ganglion cells**. Because neural crest cells migrate caudally, the **rectum is always involved**.

The absence of parasympathetic ganglia in the colonic wall causes the affected segment to be narrowed because it cannot relax. The passage of intestinal contents through this area is difficult, and compensatory dilation of the proximal colon occurs.

Newborns with Hirschsprung disease often **fail to pass meconium** within 48 hours of birth. They may also develop signs of intestinal obstruction, such as bilious vomiting and abdominal distension. The bowel is filled with stool, but the rectum is empty; anal sphincter tone is usually increased.

**(Choice A)** Degeneration of neural crest cells forming the myenteric plexus in the esophagus causes achalasia (ie, esophageal dilation with absent peristalsis). However, the condition is most often due to autoimmune destruction of mature neurons; failed neural crest migration is a very rare etiology.

**(Choices B, C, D, E, and F)** Although total colonic aganglionosis can occur, the cecum and transverse colon are not commonly involved in Hirschsprung disease. Total intestinal aganglionosis (eg, duodenum, jejunum, ileum) has also been described but is extremely rare. The rectum is most likely to be affected by a problem with neural crest cell migration, as it is at the very end of the migration path.





Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



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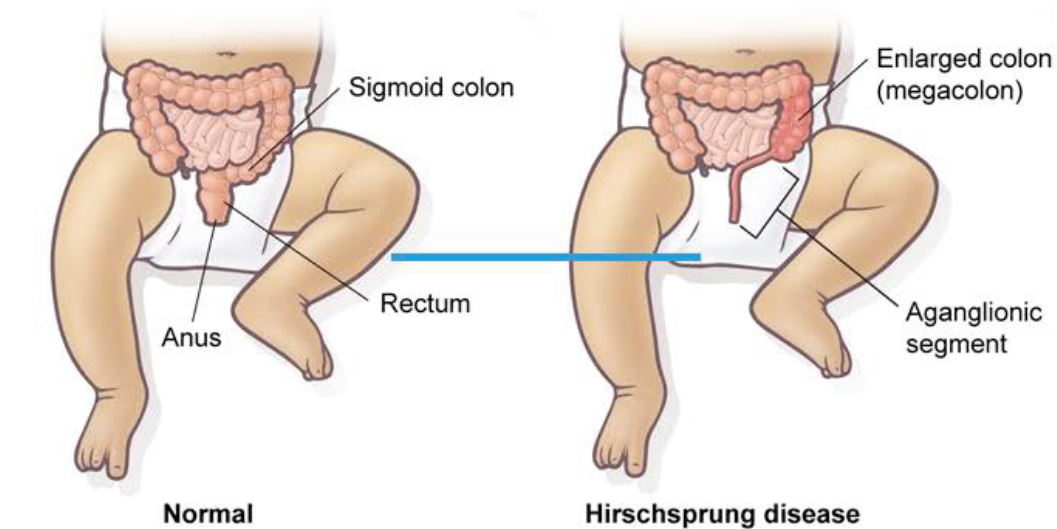
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## Exhibit Display

## Hirschsprung disease



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a problem with neural crest cell migration, as it is at the very end of the migration path.

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

develop signs of intestinal obstruction, such as bilious vomiting and abdominal distension. The bowel is filled with stool, but the rectum is empty; anal sphincter tone is usually increased.

**(Choice A)** Degeneration of neural crest cells forming the myenteric plexus in the esophagus causes achalasia (ie, esophageal dilation with absent peristalsis). However, the condition is most often due to autoimmune destruction of mature neurons; failed neural crest migration is a very rare etiology.

**(Choices B, C, D, E, and F)** Although total colonic aganglionosis can occur, the cecum and transverse colon are not commonly involved in Hirschsprung disease. Total intestinal aganglionosis (eg, duodenum, jejunum, ileum) has also been described but is extremely rare. The rectum is most likely to be affected by a problem with neural crest cell migration, as it is at the very end of the migration path.

### Educational objective:

Hirschsprung disease is caused by abnormal migration of neural crest cells (ganglion cell precursors) during embryogenesis. Because neural crest cells migrate caudally down the bowel from the foregut, the rectum is always affected.

### References

- [The developmental etiology and pathogenesis of Hirschsprung disease.](#)





A 43-year-old man comes to the office due to yellowing of the skin over the past several days. He has had no fever or abdominal pain and has not traveled recently or received blood transfusions. The patient has also experienced increased shortness of breath with exercise over the past few months. He has no other medical conditions and takes no medications. The patient drinks 1 or 2 glasses of wine on social occasions and does not use tobacco or illicit drugs. His father died of liver cirrhosis attributed to alcohol use. On physical examination, expiration is prolonged and there are scattered bilateral wheezes. Laboratory results show total bilirubin of 4.1 mg/dL and alanine aminotransferase of 90 U/L. Viral hepatitis serology is negative. Chest x-ray shows hyperlucency of lung fields and flattening of the diaphragm. Abdominal ultrasound reveals increased liver span and echogenicity of the liver parenchyma but no masses. Which of the following is the most likely underlying cause of this patient's symptoms?

- ☐ A. Autoimmune injury of the intrahepatic bile ducts
- ☐ B. Decreased UDP-glucuronosyltransferase activity
- ☐ C. Defective chloride transport at epithelial surfaces
- ☐ D. Defective transport and accumulation of copper
- ☐ E. Inherited deficiency of a serine protease inhibitor





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

medical conditions and takes no medications. The patient drinks 1 or 2 glasses of wine on social occasions and does not use tobacco or illicit drugs. His father died of liver cirrhosis attributed to alcohol use. On physical examination, expiration is prolonged and there are scattered bilateral wheezes. Laboratory results show total bilirubin of 4.1 mg/dL and alanine aminotransferase of 90 U/L. Viral hepatitis serology is negative. Chest x-ray shows hyperlucency of lung fields and flattening of the diaphragm. Abdominal ultrasound reveals increased liver span and echogenicity of the liver parenchyma but no masses. Which of the following is the most likely underlying cause of this patient's symptoms?

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- ☐ B. Decreased UDP-glucuronosyltransferase activity
- ☐ C. Defective chloride transport at epithelial surfaces
- ☐ D. Defective transport and accumulation of copper
- ☐ E. Inherited deficiency of a serine protease inhibitor
- ☐ F. Unregulated gastrointestinal iron absorption

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occasions and does not use tobacco or illicit drugs. His father died of liver cirrhosis attributed to alcohol use. On physical examination, expiration is prolonged and there are scattered bilateral wheezes. Laboratory results show total bilirubin of 4.1 mg/dL and alanine aminotransferase of 90 U/L. Viral hepatitis serology is negative. Chest x-ray shows hyperlucency of lung fields and flattening of the diaphragm. Abdominal ultrasound reveals increased liver span and echogenicity of the liver parenchyma but no masses. Which of the following is the most likely underlying cause of this patient's symptoms?

- ☐ A. Autoimmune injury of the intrahepatic bile ducts (8%)
- ☐ B. Decreased UDP-glucuronosyltransferase activity (10%)
- ☐ C. Defective chloride transport at epithelial surfaces (4%)
- ☐ D. Defective transport and accumulation of copper (4%)
- ☒ E. Inherited deficiency of a serine protease inhibitor (67%)
- ☐ F. Unregulated gastrointestinal iron absorption (4%)

Correct

67%



01 min, 09 secs



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Previous



Next



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Lab Values



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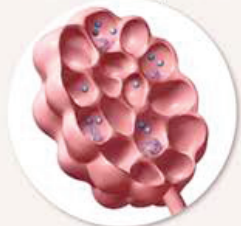
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## Exhibit Display

## Alpha-1 antitrypsin deficiency

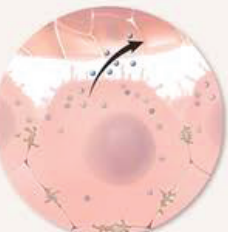
## Normal

Alpha-1 antitrypsin protects alveoli from neutrophil elastase

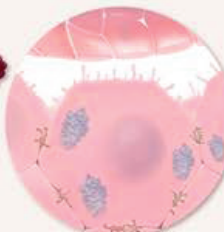


## Affected

Alveolar destruction by neutrophil elastase

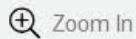


Alpha-1 antitrypsin released from hepatocytes



Alpha-1 antitrypsin accumulation in hepatocytes

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End Block



Mark



Previous



Next



Full Screen



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Notes



Calculator



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This patient with signs of liver dysfunction (ie, jaundice, transaminitis) and evidence of **emphysema** on chest x-ray (eg, hyperlucency, diaphragmatic flattening) likely has **alpha-1 antitrypsin deficiency** (AATD).

Alpha-1 antitrypsin is a **serine protease inhibitor** that regulates the activity of a number of tissue-destructive proteases, most importantly neutrophil **elastase**. Deficiency is inherited in an autosomal codominant fashion.

AATD leads to unchecked elastase activity in the lungs, resulting in alveolar destruction and lung hyperinflation; the panacinar emphysema tends to favor the basilar lung regions and typically develops prior to age 50. In addition, some patients can develop **liver disease** due to accumulation of improperly folded alpha-1 antitrypsin proteins in hepatocytes. Liver disease is of greatest concern in the first 2 decades of life, but it can present in any decade. Patients can experience hepatomegaly, hyperbilirubinemia, elevated transaminases, and eventual cirrhosis and end-stage liver disease. Hepatocellular carcinoma may also develop.

**(Choice A)** Autoimmune injury of intrahepatic bile ducts occurs in primary biliary cholangitis (PBC, formerly primary biliary cirrhosis). PBC predominantly affects women and is characterized by positive antimitochondrial antibodies. It is not associated with emphysema.



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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**(Choice B)** UDP-glucuronosyltransferase is an enzyme that converts unconjugated bilirubin to its conjugated form, and inherited deficiency can exist in varying degrees. Mild deficiency results in benign elevations in unconjugated bilirubin during periods of stress (ie, Gilbert syndrome), while severe deficiency can be fatal during infancy (ie, Crigler-Najjar syndrome type I).

**(Choice C)** Defective epithelial chloride transport occurs in cystic fibrosis. Patients typically develop obstructive lung disease in the form of bronchiectasis and can have pancreatic insufficiency leading to malabsorption. In addition, cirrhosis can sometimes occur. Cystic fibrosis usually presents during childhood; onset of disease manifestations at age >40 would be highly unusual.

**(Choice D)** Defective copper transport resulting in accumulation of intracellular copper occurs in Wilson disease. Patients can develop cirrhosis as well as brain degeneration leading to neurologic (eg, dysarthria, gait abnormalities) and psychiatric (eg, impulsivity) manifestations.

**(Choice F)** Unregulated gastrointestinal iron absorption occurs in hemochromatosis. Patients can develop cirrhosis due to iron overload. The joints (arthritis), pancreas (diabetes mellitus), and heart (cardiomyopathy) are also commonly affected, but lung involvement is not typical.

**Educational objective:**

Alpha 1 antitrypsin (AAT) is a serine protease inhibitor that regulates the activity of elastase in the lung.

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Feedback



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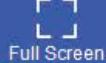
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Mark

Previous

Next



Full Screen



Tutorial



Lab Values



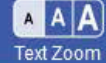
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**(Choice C)** Defective epithelial chloride transport occurs in cystic fibrosis. Patients typically develop obstructive lung disease in the form of bronchiectasis and can have pancreatic insufficiency leading to malabsorption. In addition, cirrhosis can sometimes occur. Cystic fibrosis usually presents during childhood; onset of disease manifestations at age >40 would be highly unusual.

**(Choice D)** Defective copper transport resulting in accumulation of intracellular copper occurs in Wilson disease. Patients can develop cirrhosis as well as brain degeneration leading to neurologic (eg, dysarthria, gait abnormalities) and psychiatric (eg, impulsivity) manifestations.

**(Choice F)** Unregulated gastrointestinal iron absorption occurs in hemochromatosis. Patients can develop cirrhosis due to iron overload. The joints (arthritis), pancreas (diabetes mellitus), and heart (cardiomyopathy) are also commonly affected, but lung involvement is not typical.

### **Educational objective:**

Alpha-1 antitrypsin (AAT) is a serine protease inhibitor that regulates the activity of elastase in the lung. Inherited deficiency of AAT leads to alveolar destruction and panacinar emphysema; in addition, accumulation of improperly folded AAT proteins in hepatocytes can lead to liver dysfunction and cirrhosis in some patients.



1



Feedback



Suspend



End Block



A 42-year-old woman comes to the office due to frequent episodes of burning in her chest and small amounts of regurgitation after meals and at nighttime. Medical history includes hypertension. Vital signs are within normal limits. BMI is 30 kg/m<sup>2</sup>. There is no abdominal tenderness and the remainder of the physical examination is normal. The patient shows the clinician an over-the-counter antacid that she has been taking to relieve her symptoms. The preparation contains a combination of magnesium and aluminum hydroxide. Which of the following is the most likely rationale for combining both mineral salts in this antacid preparation?

- ☐ A. Improve systemic absorption
- ☐ B. Minimize drug interactions
- ☐ C. Prevent rebound acid secretion
- ☐ D. Reduce adverse effects
- ☐ E. Reduce the risk of alkalosis and renal failure

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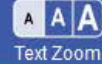
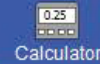
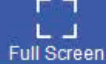


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A 42-year-old woman comes to the office due to frequent episodes of burning in her chest and small amounts of regurgitation after meals and at nighttime. Medical history includes hypertension. Vital signs are within normal limits. BMI is 30 kg/m<sup>2</sup>. There is no abdominal tenderness and the remainder of the physical examination is normal. The patient shows the clinician an over-the-counter antacid that she has been taking to relieve her symptoms. The preparation contains a combination of magnesium and aluminum hydroxide. Which of the following is the most likely rationale for combining both mineral salts in this antacid preparation?

- ☐ A. Improve systemic absorption (9%)
- ☐ B. Minimize drug interactions (3%)
- ☐ C. Prevent rebound acid secretion (19%)
- ☒ D. Reduce adverse effects (55%)
- ☐ E. Reduce the risk of alkalosis and renal failure (12%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Magnesium salts (eg, magnesium trisilicate, magnesium hydroxide) and aluminum hydroxide are **weak alkali mineral salts**. They temporarily **increase the gastric pH** by neutralizing hydrochloric acid, helping to **relieve gastroesophageal reflux** symptoms.

**Aluminum** hydroxide has a tendency to cause **constipation** due to interactions with intestinal secretions that form insoluble salts. In contrast, **magnesium** salts cause osmotic **diarrhea**. Therefore, the two medications are combined to offset the adverse effects of the individual medications. Patients with reflux symptoms and chronic constipation may benefit from magnesium salt monotherapy, whereas aluminum hydroxide monotherapy may be of value in patients with chronic diarrhea.

**(Choice A)** Aluminum, when absorbed in large doses, causes osteomalacia, bone pain, hypercalcemia, and dementia. Aluminum absorption in the gastrointestinal tract is minimal from the salt form, and toxicity tends to occur in patients with chronic kidney disease that limits renal excretion. Combination therapy does not alter systemic absorption.

**(Choice B)** Drug interactions are common with antacid medications, largely due to pH-related changes in protein binding, absorption, or elimination of the drugs. Combining multiple alkalinizing agents would not minimize their effects on other drugs.



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice B)** Drug interactions are common with antacid medications, largely due to pH-related changes in protein binding, absorption, or elimination of the drugs. Combining multiple alkalinizing agents would not minimize their effects on other drugs.

**(Choice C)** Rebound acid hypersecretion can occur with calcium carbonate, magnesium hydroxide, aluminum hydroxide, and proton pump inhibitors. This is likely due to increased gastrin release as a result of gastric alkalization or (in the case of calcium salts) direct ionic stimulation.

**(Choice E)** Milk-alkali syndrome is caused by excessive use of calcium carbonate antacids and is characterized by hypercalcemia, alkalosis, and renal dysfunction. Kidney injury occurs due to both hypercalcemia-induced renal vasoconstriction and calcium-induced diuresis. The resultant volume depletion, decreased glomerular filtration rate, and alkali intake lead to a metabolic alkalosis. However, severe alkalosis can occur with all antacids, and the combination of magnesium and aluminum would not decrease this risk.

**Educational objective:**

Magnesium salts and aluminum hydroxide are basic mineral salts used to neutralize gastric acid and relieve gastroesophageal reflux symptoms. Side effects include diarrhea and constipation, respectively. Therefore, these medications are often combined to offset the adverse effects of the individual medications.







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

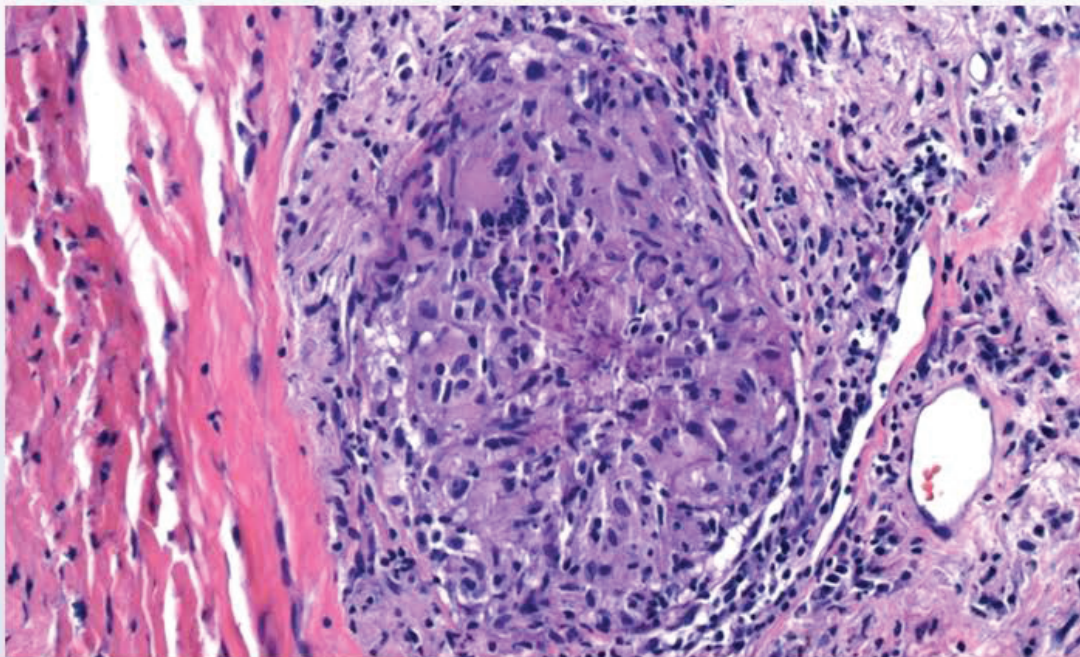


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A 32-year-old man with abdominal pain and periodic diarrhea is found to have heme-positive stools. Stool cultures show no growth of pathogenic organisms. Colonoscopy with biopsy of the colonic mucosa is performed. Light microscopy of the tissue sample is shown in the image below.



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Feedback



Suspend



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

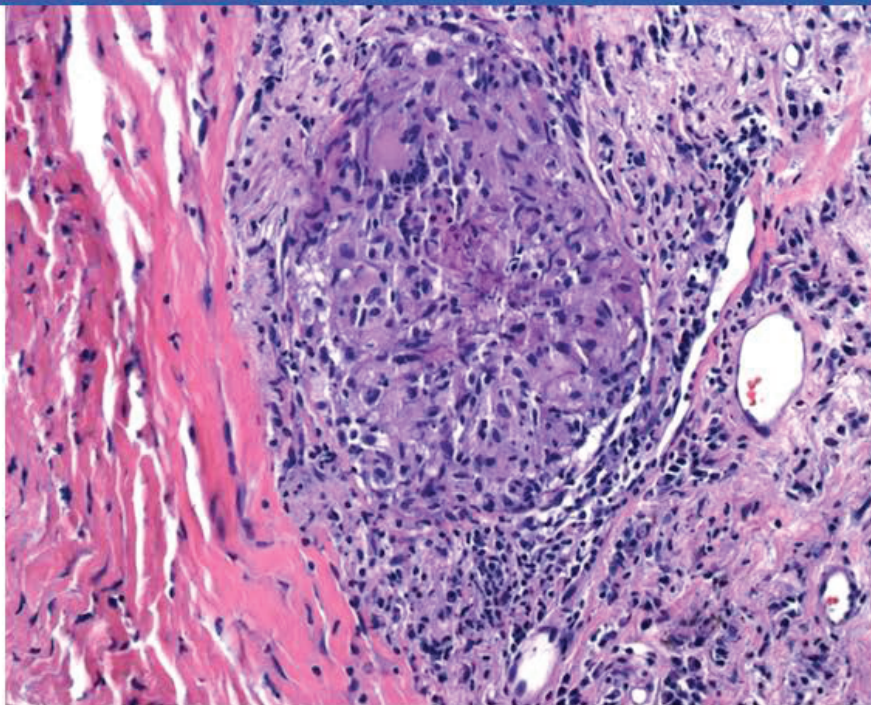
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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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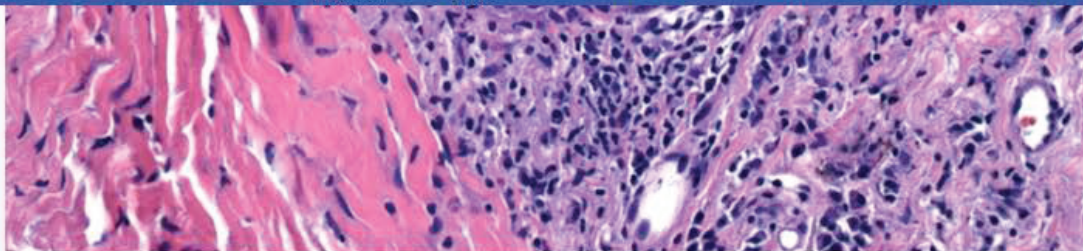
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Settings



This patient most likely suffers from which of the following disorders?

- ☐ A. Acute appendicitis
- ☐ B. Collagenous colitis
- ☐ C. Crohn disease
- ☒ D. Ischemic colitis
- ☐ E. Pseudomembranous colitis
- ☐ F. Ulcerative colitis

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

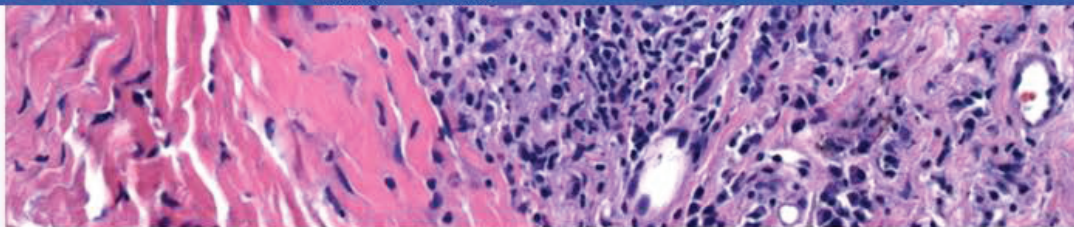
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This patient most likely suffers from which of the following disorders?

- ☐ A. Acute appendicitis (0%)
- ☐ B. Collagenous colitis (3%)
- ☒ C. Crohn disease (75%)
- ☐ D. Ischemic colitis (1%)
- ☐ E. Pseudomembranous colitis (1%)
- ☐ F. Ulcerative colitis (18%)

Correct

75%  
Answered correctly29 secs  
Time spent01/08/2021  
Last updated

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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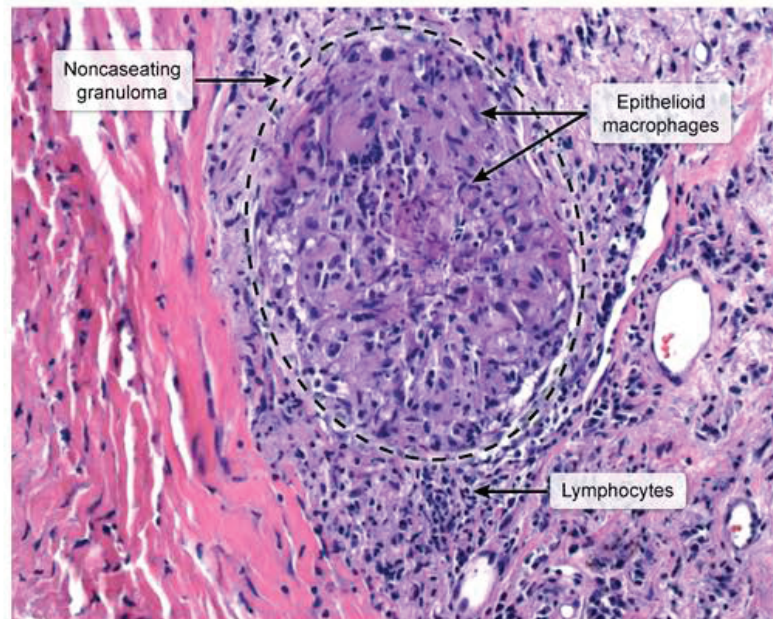
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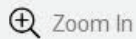
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## Exhibit Display

## Noncaseating granuloma



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Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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This younger patient with abdominal pain, heme-positive stool, and **noncaseating granulomas** (NCGs, pictured above) on microscopy has **Crohn disease** (CD). CD is an inflammatory bowel disease that can cause patchy inflammation throughout the gastrointestinal tract, interspersed with areas of normal bowel (**skip lesions**).

NCGs are often seen in CD and are considered a hallmark of the disease. NCGs are characterized by an accumulation of epithelioid macrophages that frequently form multinucleated giant cells without central necrosis (noncaseating), surrounded by a cuff of lymphocytes. Granulomas are formed in an attempt to wall off an offending agent; in the case of CD this is likely due to an unregulated immune response to gut flora or self-antigens. They can be found in any layer of the intestinal wall, and may also be present in other tissues such as the lymph nodes and skin. Other characteristic histopathologic findings in CD include inflammation involving the entire thickness of the intestinal wall (**transmural inflammation**), distortion of normal mucosal architecture, and Paneth cell metaplasia.

**(Choice A)** *Acute appendicitis* presents with periumbilical or right lower quadrant pain and fever.

Microscopy shows a dense neutrophilic infiltrate and necrosis of the appendix.

**(Choice B)** *Collagenous (microscopic) colitis* typically presents with frequent diarrhea in older women and



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(Choice A) Acute appendicitis presents with periumbilical or right lower quadrant pain and fever.

Microscopy shows a dense neutrophilic infiltrate and necrosis of the appendix.

(Choice B) Collagenous (microscopic) colitis typically presents with frequent diarrhea in older women and histology demonstrates thickening of the subepithelial collagen band.

(Choice D) Ischemic colitis is most common in older patients and presents with abdominal pain and bleeding; microscopy shows necrosis, thrombus formation, and hemorrhage.

(Choice E) Pseudomembranous colitis is due to *Clostridioides difficile* infection and presents with watery diarrhea, abdominal pain, and fever. Microscopy shows mucopurulent exudates composed of fibrin, bacteria, and neutrophils.

(Choice F) Ulcerative colitis is another cause of inflammatory bowel disease; histology demonstrates a continuous superficial inflammation affecting the mucosa and submucosa with crypt abscesses (neutrophil collections within glandular lumen) and crypt atrophy. Granulomas do not occur.

### Educational objective:

Noncaseating granulomas are a hallmark of Crohn disease and can help distinguish it from ulcerative colitis, which does not form granulomas. Histopathology in Crohn disease also demonstrates transmural inflammation, distortion of the normal architecture, and Paneth cell metaplasia.





Mark



Previous



Next



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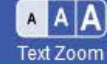
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**(Choice D)** Ischemic colitis is most common in older patients and presents with abdominal pain and bleeding; microscopy shows necrosis, thrombus formation, and hemorrhage.

**(Choice E)** Pseudomembranous colitis is due to *Clostridioides difficile* infection and presents with watery diarrhea, abdominal pain, and fever. Microscopy shows mucopurulent exudates composed of fibrin, bacteria, and neutrophils.

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Noncaseating granulomas are a hallmark of Crohn disease and can help distinguish it from ulcerative colitis, which does not form granulomas. Histopathology in Crohn disease also demonstrates transmural inflammation, distortion of the normal architecture, and Paneth cell metaplasia.

Pathology

Subject

Gastrointestinal &amp; Nutrition

System

Inflammatory bowel disease

Topic

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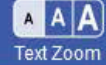
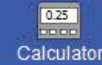
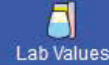
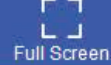
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A 52-year-old man is brought to the emergency department for hematemesis that began an hour earlier. He has regularly consumed large amounts of alcohol for the last 20 years and has been hospitalized numerous times due to ethanol intoxication. Temperature is 36.7 C (98 F), blood pressure is 90/60 mm Hg, pulse is 106/min, and respirations are 22/min. Physical examination shows jaundice and scleral icterus. Examination of the abdomen reveals a palpable spleen and moderate ascites. Endoscopy reveals bleeding esophageal varices. This patient's current condition most likely resulted from chronic shunting of blood through which of the following veins?

- ☐ A. Left gastric
- ☐ B. Middle colic
- ☐ C. Paraumbilical
- ☐ D. Right gastroepiploic
- ☐ E. Splenic
- ☐ F. Superficial epigastric





He has regularly consumed large amounts of alcohol for the last 20 years and has been hospitalized numerous times due to ethanol intoxication. Temperature is 36.7 C (98 F), blood pressure is 90/60 mm Hg, pulse is 106/min, and respirations are 22/min. Physical examination shows jaundice and scleral icterus. Examination of the abdomen reveals a palpable spleen and moderate ascites. Endoscopy reveals **bleeding esophageal varices**. This patient's current condition most likely resulted from chronic shunting of blood through which of the following veins?

- ☒ A. Left gastric (71%)
- ☐ B. Middle colic (0%)
- ☐ C. Paraumbilical (5%)
- ☐ D. Right gastroepiploic (5%)
- ☐ E. Splenic (10%)
- ☐ F. Superficial epigastric (6%)

Correct

71%  
Answered correctly18 secs  
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Next

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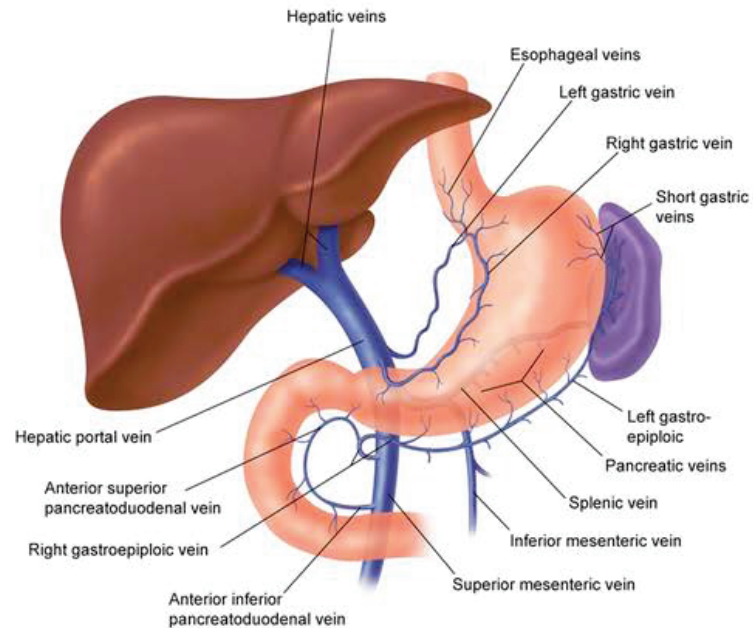
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## Exhibit Display

## Veins of stomach



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Previous



Next



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This patient has numerous cirrhotic stigmata including ascites, jaundice, and splenomegaly. An important cause of cirrhosis-related morbidity and mortality is the development of **variceal hemorrhaging** as a direct consequence of portal hypertension.

**Cirrhosis** (of any type) represents the end stage of progressive hepatic fibrosis. It is characterized by distortion of the hepatic architecture and formation of regenerative nodules. Cirrhosis is the most common cause of **portal hypertension**, which arises from increased resistance to portal flow at the hepatic sinusoids. Chronic portal hypertension leads to dilation of small, pre-existing vascular channels between the portal and systemic circulations. These dilated collateral vessels (**portosystemic anastomoses**) commonly form in the anterior abdomen (caput medusae), lower rectum (anorectal varices), and **inferior end of the esophagus** (esophageal varices).

Treatment sometimes includes inserting a transjugular intrahepatic portosystemic shunt (TIPS) between the portal vein and hepatic vein percutaneously, relieving portal hypertension by shunting blood to the systemic circulation.

**(Choice B)** The middle colic vein drains the transverse colon.

**(Choices C and F)** In cirrhosis, the paraumbilical veins can shunt blood from the portal system to



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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**(Choice B)** The middle colic vein drains the transverse colon.

**(Choices C and F)** In cirrhosis, the paraumbilical veins can shunt blood from the portal system to superficial epigastric veins in the abdominal wall, causing **caput medusae**.

**(Choice D)** The right gastroepiploic vein drains venous blood from the inferior portions of the stomach. It runs along the greater curvature of the stomach.

**(Choice E)** The splenic vein drains blood from the spleen. It joins with the superior mesenteric vein to form the hepatic portal vein. Patients with portal hypertension can develop splenomegaly due to congestion of the splenic red pulp.

### Educational objective:

In cirrhosis, portal hypertension arises from increased resistance to portal flow at the hepatic sinusoids. This causes increased pressure in the portosystemic collateral veins within the lower end of the esophagus, anterior abdomen, and lower rectum. Dilation of these collateral vessels is responsible for the esophageal varices, caput medusae, and anorectal varices commonly seen in patients with cirrhosis.

Anatomy

Gastrointestinal &amp; Nutrition

Cirrhosis

Subject

System

Topic

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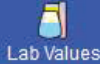
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Tutorial



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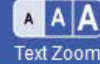
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A 47-year-old morbidly obese woman comes to the physician seeking advice regarding weight loss. She has tried diet and exercise a number of times without success. Her other medical problems include type 2 diabetes mellitus and obstructive sleep apnea. Her body mass index is  $43 \text{ kg/m}^2$ . After a discussion about available surgical options, she expresses interest in the adjustable gastric band, an inflatable silicone device that is placed around the cardiac part of the stomach. In order to encircle the stomach, the band must pass through which of the following structures?

- ☐ A. Falciform ligament
- ☐ B. Gastrocolic ligament
- ☐ C. Greater omentum
- ☐ D. Lesser omentum
- ☐ E. Splenorenal ligament

**Submit**

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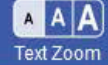
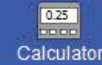
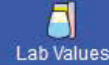
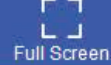
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A 47-year-old morbidly obese woman comes to the physician seeking advice regarding weight loss. She has tried diet and exercise a number of times without success. Her other medical problems include type 2 diabetes mellitus and obstructive sleep apnea. Her body mass index is 43 kg/m<sup>2</sup>. After a discussion about available surgical options, she expresses interest in the adjustable gastric band, an inflatable silicone device that is placed around the cardiac part of the stomach. In order to encircle the stomach, the band must pass through which of the following structures?

- ☐ A. Falciform ligament (4%)
- ☐ B. Gastrocolic ligament (14%)
- ☐ C. Greater omentum (18%)
- ☒ D. Lesser omentum (60%)
- ☐ E. Splenorenal ligament (2%)

Correct

60%  
Answered correctly

10 secs  
Time Spent

12/22/2020  
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Previous

Next

Full Screen

Tutorial

Lab Values

Notes

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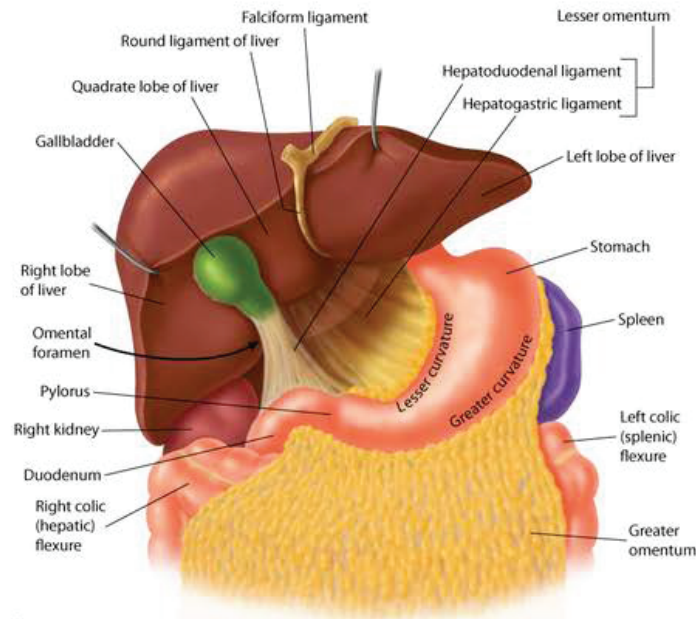
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## Greater &amp; lesser omentum



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**Adjustable gastric banding** is a type of restrictive bariatric surgery designed for obese patients. The adjustable gastric band is an inflatable silicone device placed around the gastric cardia. It is intended to slow the passage of food, increasing satiety and limiting the amount of food consumed. To encircle the upper stomach, the gastric band must pass through the lesser omentum.

The lesser omentum is a double layer of peritoneum that extends from the liver to the lesser curvature of the stomach and the beginning of the duodenum. Anatomically, the lesser omentum is divided into 2 ligaments:

1. Hepatogastric ligament: the portion connecting to the lesser curvature of the stomach
2. Hepatoduodenal ligament: the portion connecting to the duodenum

Between the 2 layers of the lesser omentum, close to the right-sided free margin, lie the hepatic artery, common bile duct, portal vein, lymphatics, and hepatic plexus. The right and left gastric arteries and gastric veins also lie between the 2 layers, near where the lesser omentum attaches to the stomach.

**(Choice A)** The falciform ligament attaches the liver to the anterior body wall. It is a derivative of the embryonic ventral mesentery and contains the round ligament, the remnant of the fetal umbilical vein.

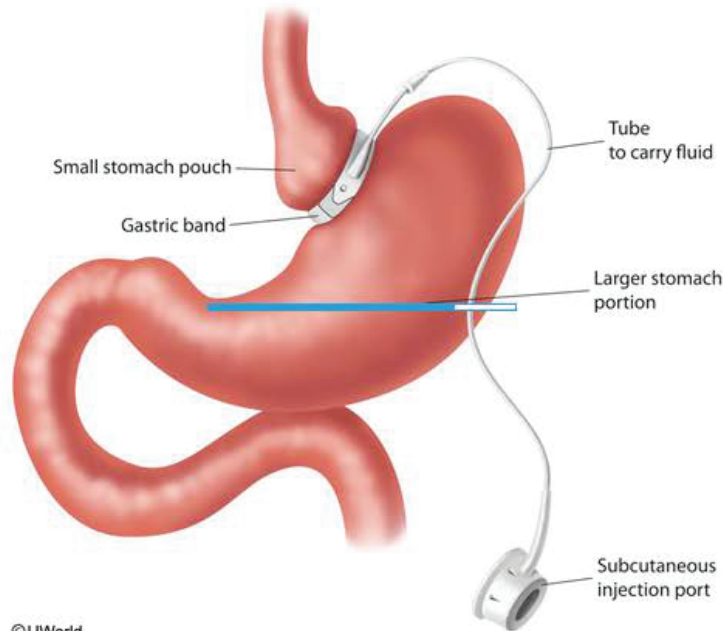
**(Choices B and C)** The greater omentum is a large fold of visceral peritoneum that extends from the greater curvature of the stomach, travels inferiorly over the small intestine, and then reflects on itself and



Adjustable gastric banding is a type of restrictive bariatric surgery designed for obese patients. The

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Adjustable gastric band



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greater curvature of the stomach, travels inferiorly over the small intestine, and then reflects on itself and

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Previous



Next



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**(Choices B and C)** The greater omentum is a large fold of visceral peritoneum that extends from the greater curvature of the stomach, travels inferiorly over the small intestine, and then reflects on itself and ascends to encompass the transverse colon before reaching the posterior abdominal wall. The gastrocolic ligament is the section that stretches from the greater curvature of the stomach to the transverse colon. It forms part of the anterior wall of the lesser sac and is often divided during surgery to provide access to the anterior pancreas and posterior wall of the stomach.

**(Choice E)** The splenorenal ligament is derived from the peritoneum and lies between the left kidney and the spleen. It contains the splenic vessels and the tail of the pancreas.

### Educational objective:

The lesser omentum is a double layer of peritoneum that extends from the liver to the lesser curvature of the stomach and the beginning of the duodenum. It is divided into the hepatogastric and hepatoduodenal ligaments.

Anatomy  
Subject

Gastrointestinal & Nutrition  
System

Obesity  
Topic

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Many drugs and toxins act by inhibiting substance flow across cell membranes. Which of the following inhibits primary active transport?

- ☐ A. Tetrodotoxin
- ☐ B. Verapamil
- ☐ C. Omeprazole
- ☐ D. Lidocaine
- ☐ E. Dofetilide

Submit





Many drugs and toxins act by inhibiting substance flow across cell membranes. Which of the following inhibits primary active transport?

- ☐ A. Tetrodotoxin (12%)
- ☐ B. Verapamil (5%)
- ☒ C. Omeprazole (70%)
- ☐ D. Lidocaine (7%)
- ☐ E. Dofetilide (3%)

Correct



70%

Answered correctly



15 secs

Time Spent



02/17/2021

Last Updated

Explanation







Transport of ions or molecules across cell membranes can be either passive (along the concentration gradient) or active (against the concentration gradient). The former does not require energy, while the latter utilizes energy from ATP. In primary active transport, the carrier molecules are enzymes that hydrolyze ATP (ATPases) and use the energy released to transport ions and molecules against their concentration gradients. Examples of such carriers are the Na/K ATPase, the H/K ATPase, and the Ca ATPase.

Synthesis of HCl by parietal cells of the gastric mucosa is dependent on the H/K ATPase, which is known as a proton pump. This carrier transports hydrogen ions into the gastric lumen in exchange for potassium ions.

Omeprazole and other proton pump inhibitors inhibit the H/K ATPase, thus decreasing the concentration of HCl in the gastric lumen. These medications are used for treatment of peptic ulcer disease, gastroesophageal reflux disease (GERD), and diseases associated with increased gastrin secretion such as the Zollinger-Ellison syndrome.

**(Choice A)** Tetrodotoxin, a potent neurotoxin found in pufferfish, functions by blocking the voltage-gated sodium channels in nerve cell membranes. It inhibits passive transport of sodium.

**(Choice B)** Verapamil blocks L-type calcium channels, thus inhibiting passive transport of calcium ions in





as the Zollinger-Ellison syndrome.

**(Choice A)** Tetrodotoxin, a potent neurotoxin found in pufferfish, functions by blocking the voltage-gated sodium channels in nerve cell membranes. It inhibits passive transport of sodium.

**(Choice B)** Verapamil blocks L-type calcium channels, thus inhibiting passive transport of calcium ions in cardiomyocytes.

**(Choice D)** Lidocaine is a local anesthetic and a class IB antiarrhythmic agent that functions by blocking voltage-gated sodium channels in sensory neurons, Purkinje fibers and ventricular cells.

**(Choice E)** Dofetilide is a class III antiarrhythmic drug that blocks passive transport of potassium, specifically the delayed outward rectifier potassium current, in cardiomyocytes leading to a prolongation of the refractory period and of the QT interval.

### Educational Objective:

Parietal cells release hydrogen ions into the gastric lumen by means of the H/K ATPase, which requires hydrolysis of ATP and is therefore an active transport mechanism. Omeprazole and other proton pump inhibitors suppress the activity of the gastric parietal cell H/K ATPase leading to an increase in the pH of the gastric lumen.





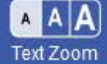
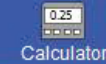
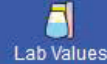
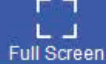
A 62-year-old man comes to the physician due to intermittent groin pain. The pain is most severe when the patient lifts heavy loads and after a long day at his job as a construction worker. Physical examination shows a right-sided groin bulge directly above the inguinal ligament. The bulge increases in size when he bears down. An ultrasound reveals that the mass originates medial to the inferior epigastric vessels. This patient's condition is most likely caused by which of the following?

- ☐ A. Failure of the internal inguinal ring to close
- ☐ B. Patent processus vaginalis
- ☐ C. Separation of the abdominal muscles
- ☐ D. Weakness of the transversalis fascia
- ☐ E. Widening of the femoral ring

Submit







A 62-year-old man comes to the physician due to intermittent **groin** pain. The pain is most severe when the patient lifts heavy loads and after a long day at his job as a construction worker. Physical examination shows a right-sided **groin bulge** directly above the inguinal ligament. The bulge increases in size when he bears down. An ultrasound reveals that the mass originates **medial** to the inferior epigastric vessels. This patient's condition is most likely caused by which of the following?

- ☐ A. Failure of the internal inguinal ring to close (3%)
- ☐ B. Patent processus vaginalis (5%)
- ☐ C. Separation of the abdominal muscles (5%)
- ☒ D. Weakness of the transversalis fascia (83%)
- ☐ E. Widening of the femoral ring (1%)

Correct

83%  
Answered correctly

51 secs  
Time Spent

11/09/2020  
Last Updated





### Groin hernias

Type	Classic presentation	Pathophysiology	Anatomy
Indirect inguinal	Male infants	Patent processus vaginalis	<ul style="list-style-type: none"><li>• Originates lateral to inferior epigastric vessels</li><li>• Protrudes through the deep inguinal ring into inguinal canal</li><li>• May extend into the scrotum (following spermatic cord)</li></ul>
Direct inguinal	Older men	Weakness of transversalis fascia	<ul style="list-style-type: none"><li>• Protrudes medial to the inferior epigastric vessels into Hesselbach's triangle</li><li>• May pass through superficial inguinal ring</li><li>• No direct route into the scrotum</li></ul>



			<ul style="list-style-type: none"> <li>No direct route into the scrotum</li> </ul>
<b>Femoral</b>	Women	Widening of the femoral ring	<ul style="list-style-type: none"> <li>Emerges inferior to inguinal ligament</li> <li>Protrudes through the femoral ring into the femoral canal</li> </ul>

Direct and indirect **inguinal hernias** are both located **above the inguinal ligament**. They can be differentiated by their side of origination in relation to the inferior epigastric vessels. Direct inguinal hernias originate medial to the inferior epigastric vessels, while indirect inguinal hernias originate lateral to the inferior epigastric vessels.

This patient's groin mass originating **medial** to the inferior epigastric vessels is characteristic of a **direct inguinal hernia** in the **Hesselbach triangle**. The transversalis fascia makes up the floor of the triangle, and **defects or weakness** involving the **transversalis fascia** can lead to protrusion of abdominal contents. Failure of this fascial layer is most often due to acquired connective tissue abnormalities or chronic abdominal wall injury (most commonly in older men).

Unlike indirect inguinal hernias, direct inguinal hernias do not pass through the internal (deep) inguinal ring but only through the external (superficial) inguinal ring. As a result, they do not have a direct route to the scrotum.

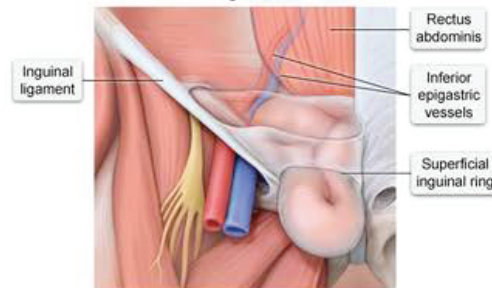




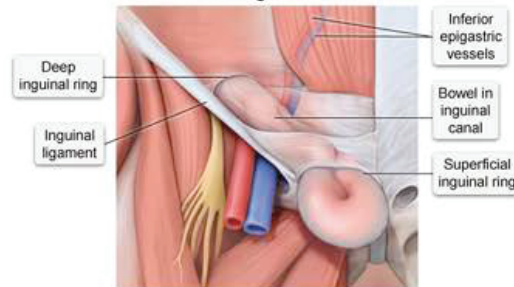
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## Inguinal hernias

## Direct inguinal hernia



## Indirect inguinal hernia



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Scrotum.

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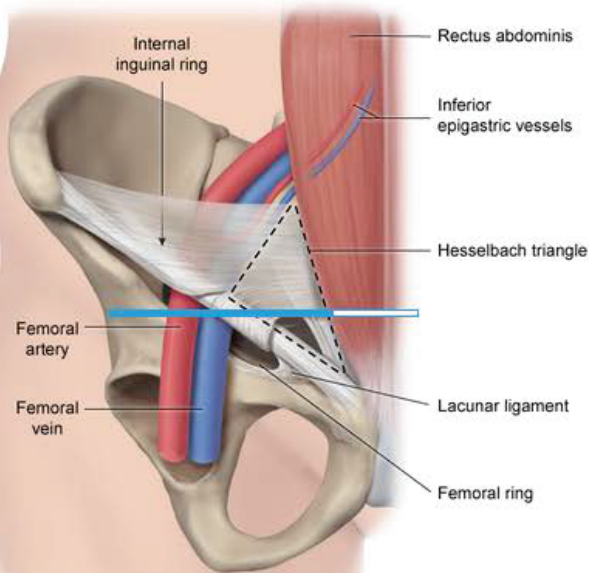
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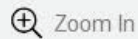
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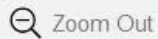
## Groin hernias



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scrotum.

**(Choices A and B)** Indirect inguinal hernias are the most common type of groin hernia in both sexes. The underlying etiology is usually congenital; due to failure of the processus vaginalis to obliterate (in males) or of the deep inguinal ring to close (in females). Indirect inguinal hernias protrude through the internal inguinal ring, lateral to the inferior epigastric vessels, allowing them to follow the same path as the spermatic cord through the inguinal canal and into the scrotum.

**(Choice C)** [Diastasis rectus abdominus](#) is characterized by an abnormally large separation between the rectus abdominus muscles due to stretching and laxity of the linea alba. This usually occurs in states with increased intraabdominal pressure (eg, pregnancy, obesity) and characteristically presents with a bulge in the midline around the umbilicus (rather than in the groin directly above the inguinal ligament).

**(Choice E)** [Femoral hernias](#) occur mainly in older women due to laxity and widening of the femoral ring, which allows abdominal contents to protrude below the inguinal ligament into the femoral canal.

### Educational objective:

Direct inguinal hernias occur most commonly in older men due to weakness of the transversalis fascia. They protrude medial to the inferior epigastric vessels into the Hesselbach triangle and pass only through the superficial inguinal ring with no direct route to the scrotum.

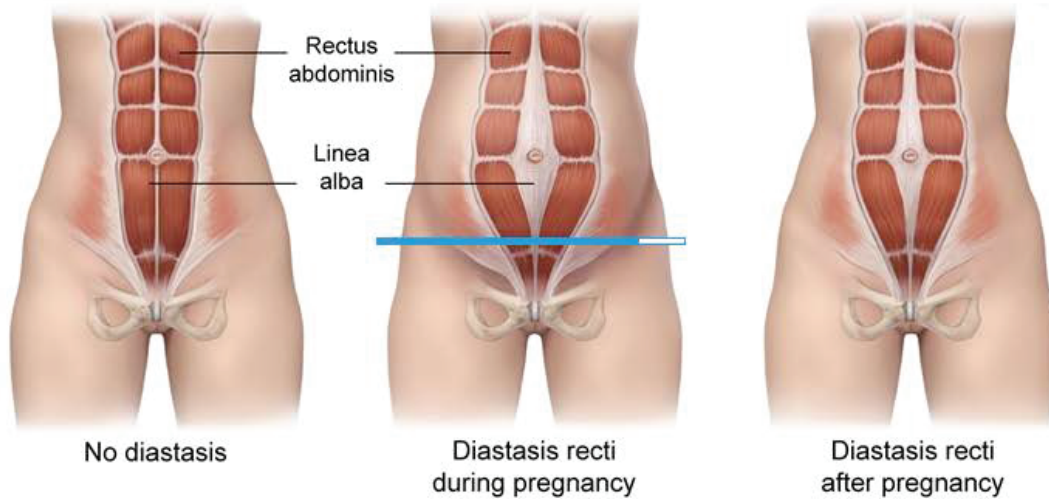






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## Diastasis recti abdominis



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Item 2 of 40

Question Id: 8669



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Previous

Next

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Tutorial

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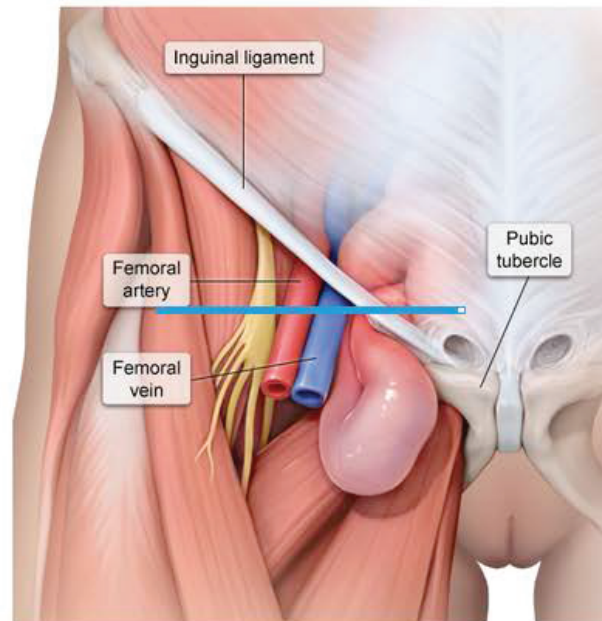
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#### Femoral hernia



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A 62-year-old man comes to the emergency department due to severe colicky upper abdominal pain, nausea, and vomiting. He reports several episodes of similar abdominal discomfort in the past. The patient does not use tobacco, alcohol, or illicit drugs. He immigrated to the United States from East Asia several years ago. Physical examination shows right upper quadrant abdominal tenderness. An imaging study shows several gallstones in the common bile duct and gallbladder. The stones are removed from the duct endoscopically, and a cholecystectomy is also performed. The gallstones are dark brown, soft, and composed primarily of calcium bilirubinate with variable amounts of cholesterol. Which of the following enzymes most likely played an important role in the pathogenesis of this patient's condition?

- ☐ A. 7-alpha-hydroxylase
- ☒ B. Aromatase
- ☐ C. Beta-glucuronidase
- ☐ D. Desmolase
- ☐ E. HMG-CoA reductase







nausea, and vomiting. He reports several episodes of similar abdominal discomfort in the past. The patient does not use tobacco, alcohol, or illicit drugs. He immigrated to the United States from East Asia several years ago. Physical examination shows right upper quadrant abdominal tenderness. An imaging study shows several gallstones in the common bile duct and gallbladder. The stones are removed from the duct endoscopically, and a cholecystectomy is also performed. The gallstones are dark brown, soft, and composed primarily of calcium bilirubinate with variable amounts of cholesterol. Which of the following enzymes most likely played an important role in the pathogenesis of this patient's condition?

- ☐ A. 7-alpha-hydroxylase (27%)
- ☐ B. Aromatase (1%)
- ☒ C. Beta-glucuronidase (45%)
- ☐ D. Desmolase (3%)
- ☐ E. HMG-CoA reductase (22%)

Correct

45%



43 secs



08/31/2020

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## Exhibit Display

## Pathogenesis of pigment stones

## Black stones

- Chronic hemolysis (eg, sickle cell, spherocytosis)
- ↑ Enterohepatic cycling of bilirubin (eg, ileal disease)

## Brown stones

- Biliary tract infection (eg, *Escherichia coli*, liver fluke)

Release of microbial  
 $\beta$ -glucuronidases

↑ Unconjugated  
bilirubin

Calcium-  
bilirubinate  
precipitation

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Gallstones can be categorized as cholesterol, pigment, or mixed stones. Cholesterol stones are formed when the ability of bile salts to solubilize cholesterol is overwhelmed by high concentrations of cholesterol in bile. Cholesterol stones are yellow to pale gray and hard. By contrast, **pigment gallstones** are composed of calcium salts of **unconjugated bilirubin**, are comparatively soft, and are dark brown to black.

**Brown** pigment stones typically arise secondary to bacterial (eg, *Escherichia coli*) or helminthic (eg, *Ascaris lumbricoides*, *Clonorchis sinensis*) **infection of the biliary tract**, which results in the release of **beta-glucuronidase** by injured hepatocytes and bacteria. This enzyme hydrolyzes bilirubin glucuronides and increases the amount of unconjugated bilirubin. The liver fluke *C sinensis* is a common cause of pigmented stones in East Asian countries and can have a prolonged quiescent phase before inducing symptoms.

Pigment stones may also occur in the absence of infection when excess bilirubin is excreted, such as with chronic **hemolytic anemia**. A small amount of conjugated bilirubin normally becomes deconjugated by endogenous beta-glucuronidase in the biliary tract. When large amounts of conjugated bilirubin are excreted into the bile, enough becomes deconjugated to promote black pigment stone formation.

(Choice A) Inhibition of 7 alpha hydroxylase (eg, fibrates) reduces the conversion of cholesterol to bile







**(Choice A)** Inhibition of 7-alpha-hydroxylase (eg, fibrates) reduces the conversion of cholesterol to bile acids and increases the risk of cholesterol stones. However, this patient's gallstones are composed primarily of unconjugated bilirubin, not cholesterol.

**(Choices B and E)** Aromatase catalyzes the conversion of androgens to estrogen, which increases hepatic cholesterol uptake. In addition, estrogens upregulate HMG Co-A reductase, which increases cholesterol synthesis. This increases biliary excretion of cholesterol, favoring formation of cholesterol stones, not pigment stones.

**(Choice D)** Desmolase (cholesterol side-chain cleavage enzyme) catalyzes the conversion of cholesterol to pregnenolone, which is the first step in the synthesis of steroid hormones.

### Educational objective:

Brown pigment gallstones are composed of calcium salts of unconjugated bilirubin and arise secondary to bacterial or helminthic infection of the biliary tract. Beta-glucuronidase released by injured hepatocytes and bacteria hydrolyzes bilirubin glucuronides to unconjugated bilirubin. The liver fluke *Clonorchis sinensis* has a high prevalence in East Asian countries and is a common cause of pigment stones.

### References

- [New pathophysiological concepts underlying pathogenesis of pigment gallstones.](#)





A 45-year-old man with diabetes mellitus is admitted to the intensive care unit due to community-acquired pneumonia, septic shock, and respiratory failure. Two days ago, he developed fever, productive cough, and shortness of breath that has progressively worsened. The patient is intubated and placed on mechanical ventilation. He is also started on intravenous fluids, broad-spectrum antibiotics, and a norepinephrine infusion. On the third day of hospitalization, hemoglobin level drops from 14 g/dL to 12 g/dL. Nasogastric suctioning reveals bright red blood. This patient's bleeding is most likely a result of which of the following processes?

- ☐ A. Autoimmune parietal cell destruction
- ☐ B. Gastrin-secreting tumor
- ☐ C. Granuloma formation
- ☐ D. *Helicobacter pylori* infection
- ☐ E. Malignant transformation
- ☐ F. Stress-related mucosal injury





pneumonia, septic shock, and respiratory failure. Two days ago, he developed fever, productive cough, and shortness of breath that has progressively worsened. The patient is intubated and placed on mechanical ventilation. He is also started on intravenous fluids, broad-spectrum antibiotics, and a norepinephrine infusion. On the third day of hospitalization, hemoglobin level drops from 14 g/dL to 12 g/dL. Nasogastric suctioning reveals bright red blood. This patient's bleeding is most likely a result of which of the following processes?

- ☐ A. Autoimmune parietal cell destruction (2%)
- ☐ B. Gastrin-secreting tumor (1%)
- ☐ C. Granuloma formation (2%)
- ☐ D. *Helicobacter pylori* infection (6%)
- ☐ E. Malignant transformation (1%)
- ☒ F. Stress-related mucosal injury (85%)

Correct

85%



39 secs



08/26/2020

Block Time Remaining: 00:02:28

TUTOR

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1



Feedback



Suspend

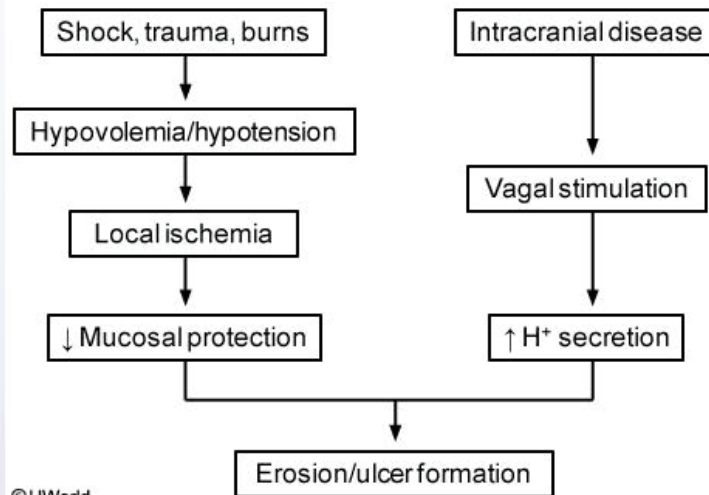


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### Stress-related mucosal disease



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**Stress-related mucosal disease** is characterized by acute gastric mucosal defects that develop in response to severe **physiologic stress** (eg, shock, extensive burns, sepsis, severe trauma, intracranial injury). Patients often have multiple, small (<1 cm), circular lesions in the stomach, ranging from superficial erosions to full-thickness ulcers. Ulcers may perforate or **bleed**, as in this patient.

The pathogenesis of these ulcers most often involves impaired mucosal protection due to **local ischemia**.





The pathogenesis of these ulcers most often involves impaired mucosal protection due to **local ischemia** caused by systemic hypotension and splanchnic vasoconstriction. Ulcers arising in the proximal duodenum in association with severe trauma/burns are called **Curling ulcers**. Ulcers arising in the esophagus, stomach, or duodenum in patients with intracranial injury are particularly prone to perforation and are called **Cushing ulcers**. Cushing ulcers are a consequence of **direct vagus nerve stimulation** caused by elevated intracranial pressure, resulting in acetylcholine release and hypersecretion of gastric acid.

**(Choice A)** Chronic gastritis with antral sparing is characteristic of autoimmune gastritis. CD4+ T cell-mediated parietal cell destruction causes impaired gastric acid and intrinsic factor secretion, resulting in achlorhydria and pernicious anemia, respectively.

**(Choice B)** Zollinger-Ellison syndrome is caused by a gastrin-secreting tumor (gastrinoma) that is usually located in the small intestine or pancreas. Patients classically have multiple peptic ulcers that may involve the distal duodenum and are more likely to respond poorly to therapy.

**(Choice C)** Granulomatous gastritis is most often idiopathic but may be associated with Crohn disease, sarcoidosis, or mycobacterial infection. It is characterized by intramucosal epithelioid granulomas that cause narrowing of the antrum secondary to transmural inflammation, which can result in gastric outlet obstruction.



obstruction.

**(Choice D)** Peptic ulcers in the stomach or duodenum are most commonly due to *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug use. *H pylori* infection is also associated with chronic antral-predominant gastritis.

**(Choice E)** Gastric adenocarcinoma can occur as the intestinal subtype (ie, bulky mass composed of glandular structures) or diffuse subtype (ie, gross stomach wall thickening with signet-ring cells on microscopy). Risk factors for gastric adenocarcinoma include chronic gastritis, cigarette smoking, *H pylori* infection, and a diet high in salt/nitrosamines.

### Educational objective:

Stress-related mucosal disease is usually caused by local ischemia in the setting of severe physiologic stress (eg, shock, extensive burns, sepsis, severe trauma). Ulcers arising in the setting of severe trauma/burns are called Curling ulcers. Ulcers arising from intracranial injury are caused by direct vagal stimulation and are called Cushing ulcers.

### References

- Stress-related mucosal disease in the intensive care unit: an update on prophylaxis.
- Stress ulceration: prevalence, pathology and association with adverse outcomes.





A 32-year-old man comes to the office due to intermittent dysphagia for solids and liquids. He has no significant past medical history and does not use tobacco, alcohol, or illicit drugs. His father has a history of esophageal squamous cell carcinoma. Physical examination is unremarkable. The patient undergoes an esophageal manometric study that demonstrates periodic, simultaneous, and non-peristaltic contractions of large amplitude and long duration. Which of the following is the most likely pathogenesis of this patient's esophageal condition?

- ☐ A. Disruption of the gastroesophageal junction
- ☐ B. Eosinophil infiltration
- ☐ C. Impaired neural inhibition
- ☐ D. Mucosal outpouching through a muscular wall defect
- ☐ E. Obstruction from unregulated cell growth
- ☐ F. Smooth muscle atrophy and gut wall fibrosis

**Submit**

Block Time Remaining: 00:02:29

TUTOR

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1



Feedback



Suspend



End Block



A 32-year-old man comes to the office due to intermittent dysphagia for solids and liquids. He has no significant past medical history and does not use tobacco, alcohol, or illicit drugs. His father has a history of esophageal squamous cell carcinoma. Physical examination is unremarkable. The patient undergoes an esophageal manometric study that demonstrates periodic, simultaneous, and non-peristaltic contractions of large amplitude and long duration. Which of the following is the most likely pathogenesis of this patient's esophageal condition?

- ☐ A. Disruption of the gastroesophageal junction (6%)
- ☐ B. Eosinophil infiltration (2%)
- ☒ C. Impaired neural inhibition (77%)
- ☐ D. Mucosal outpouching through a muscular wall defect (3%)
- ☐ E. Obstruction from unregulated cell growth (3%)
- ☐ F. Smooth muscle atrophy and gut wall fibrosis (7%)





Item 5 of 40

Question Id: 280



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



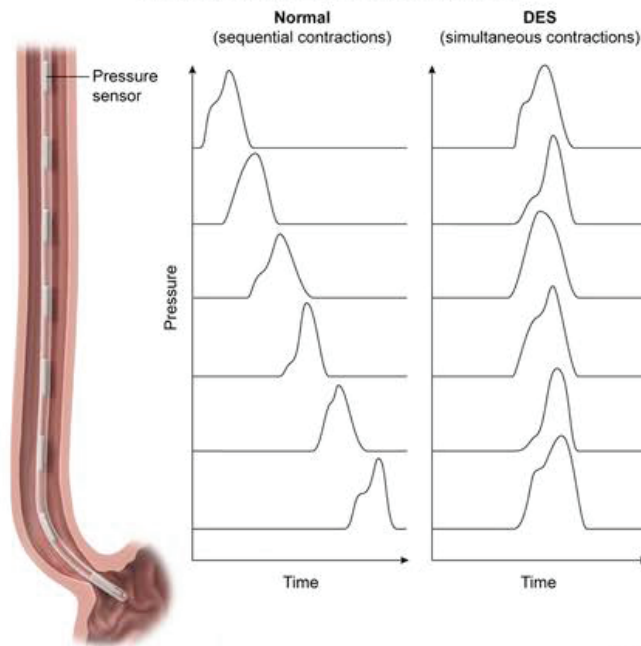
Text Zoom



Settings

## Exhibit Display

## Diffuse esophageal spasm (DES) manometry



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Zoom In



Zoom Out



Reset



New | Existing



My Notebook

Block Time Remaining: 00:03:18

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Feedback



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End Block





This patient's presentation is consistent with **diffuse esophageal spasm (DES)**. Esophageal contractions are normally stimulated by esophageal distension from a food bolus. The contractions originate above the site of distension and propel the bolus downward in a coordinated fashion. In DES, several segments of the esophagus contract inappropriately at the same time, which appears as disorganized **non-peristaltic contractions** on esophageal manometry and "corkscrew" esophagus on barium esophagogram. Because the food bolus is inefficiently propelled toward the stomach, patients typically present with intermittent **solid/liquid dysphagia, chest pain**, heartburn, and food regurgitation. The pathogenesis of DES likely involves **impaired inhibitory neurotransmission** within the esophageal myenteric plexus.

**(Choice A)** Patients with sliding hiatal hernia often develop symptoms of gastroesophageal reflux (eg, heartburn, regurgitation, dysphagia) due to anatomic disruption of the gastroesophageal junction and impaired esophageal acid clearance. However, esophageal manometry is typically normal.

**(Choice B)** Eosinophilic esophagitis typically presents in atopic patients with solid food dysphagia and/or food impaction. Findings on esophageal manometry are nonspecific.

**(Choice D)** Zenker's diverticulum is a mucosal outpouching through an area of muscle weakness located in the wall of the hypopharynx (Killian triangle). The condition typically presents in elderly men with dysphagia, foul breath (halitosis), and food regurgitation.



in the wall of the hypopharynx (Killian triangle). The condition typically presents in elderly men with dysphagia, foul breath (halitosis), and food regurgitation.

**(Choice E)** Esophageal cancer typically presents with progressive solid food dysphagia and unintentional weight loss. Risk factors for squamous cell carcinoma include alcohol and tobacco use, whereas risk factors for adenocarcinoma include Barrett's esophagus, gastroesophageal reflux disease, smoking, and obesity.

**(Choice F)** Systemic sclerosis may involve the lower two-thirds of the esophagus, resulting in smooth muscle atrophy and gut wall fibrosis. Patients can develop dysphagia with acid reflux; however, manometry typically shows absent peristaltic waves with decreased lower esophageal sphincter tone.

### Educational objective:

Diffuse esophageal spasm is characterized by periodic, simultaneous, and non-peristaltic contractions of the esophagus due to impaired inhibitory innervation within the esophageal myenteric plexus. Patients typically present with liquid/solid dysphagia and chest pain due to inefficient propulsion of food into the stomach.

### References

- [Distal esophageal spasm: an update](#)



A 32-year-old male with anorexia and fatigue is found to have persistently elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. He is also positive for HBsAg. Which of the following best describes the mechanism of liver injury in this patient?

- ☐ A. Direct viral cytotoxic effect with hepatocyte necrosis
- ☐ B. Antibody response to viral antigens on the cell surface with antibody-mediated cell damage
- ☐ C. Circulating viral antigen-antibody complexes with small vessel deposition and immunologic vessel injury
- ☐ D. Antigen mimicry with generation of self-antigen recognizing CD4+ T lymphocytes that damage hepatocytes
- ☒ E. CD8+ T lymphocyte response to viral antigens on the cell surface resulting in hepatocyte damage

Submit







A 32-year-old male with anorexia and fatigue is found to have persistently elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. He is also positive for HBsAg. Which of the following best describes the mechanism of liver injury in this patient?

- ☐ A. Direct viral cytotoxic effect with hepatocyte necrosis (26%)
- ☐ B. Antibody response to viral antigens on the cell surface with antibody-mediated cell damage (12%)
- ☐ C. Circulating viral antigen-antibody complexes with small vessel deposition and immunologic vessel injury (3%)
- ☐ D. Antigen mimicry with generation of self-antigen recognizing CD4+ T lymphocytes that damage hepatocytes (4%)
- ☒ E. CD8+ T lymphocyte response to viral antigens on the cell surface resulting in hepatocyte damage (53%)

Correct



53%

Answered correctly



01 min, 15 secs

Time Spent



01/30/2021

Last Updated

Block Time Remaining: 00:04:33

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Feedback



Suspend



End Block



Hepatitis B virus infection progresses through two phases: the proliferative phase and the integrative phase.

In the proliferative phase, the entire virion and all related antigens of the episomal HBV DNA are present. On the hepatocyte cell surface, viral HBsAg and HBcAg are expressed in conjunction with the major histocompatibility complex (MHC) class I molecules. This expression serves to activate the cytotoxic CD8+ T lymphocytes, which respond by destroying the infected hepatocytes. Note that the virion itself does not have a cytopathic effect.

In the integrative phase, the HBV DNA is incorporated into the host genome of those hepatocytes that survived the immune response. Infectivity ceases and liver damage tapers off when the antiviral antibodies appear and viral replication stops. The risk of hepatocellular carcinoma, however, remains elevated because of the HBV DNA that has been integrated into the host genome.

**(Choice A)** Hepatitis B virus has no direct cytotoxic effect.

**(Choice B)** Host antibody HBsAb neutralizes HBV infectivity by binding to the viral surface antigen HBsAg and preventing the antigen from interacting with hepatocyte receptors. Note that this neutralization occurs before the virus enters the hepatocyte, and therefore would not be associated with hepatocellular damage.





**(Choice A)** Hepatitis B virus has no direct cytotoxic effect.

**(Choice B)** Host antibody HBsAb neutralizes HBV infectivity by binding to the viral surface antigen HBsAg and preventing the antigen from interacting with hepatocyte receptors. Note that this neutralization occurs before the virus enters the hepatocyte, and therefore would not be associated with hepatocellular damage.

**(Choice C)** Antigen-antibody complexes cause some of the early symptoms of hepatitis B virus infection (eg, arthralgias, arthritis, and urticaria) as well as some of the chronic complications (eg, immune complex glomerulonephritis, cryoglobulinemia, vasculitis). These complexes are not responsible for hepatocellular damage, however.

**(Choice D)** The pathogenesis of autoimmune hepatitis (not hepatitis B infection) involves antigen mimicry with generation of self-antigen recognizing CD4+ T lymphocytes that damage hepatocytes.

### Educational Objective:

Hepatitis B virus does not have a cytotoxic effect itself; however, the presence of viral HBsAg and HBcAg on the cell surface stimulate the host's cytotoxic CD8+ T lymphocytes to destroy infected hepatocytes.

Pathophysiology

Gastrointestinal & Nutrition

Hepatitis b

Subject

System

Topic







A 23-year-old man is hospitalized with acute pancreatitis that resolves rapidly on fasting. He has suffered 2 similar episodes during the past 2 years. A gallbladder ultrasound obtained during a previous episode was normal. The patient has no other medical problems and takes no medications. He does not consume alcohol. Which of the following tests should be considered during the workup of this patient?

- ☐ A. Serum ceruloplasmin
- ☐ B. Serum cholesterol
- ☐ C. Serum ferritin
- ☐ D. Serum triglycerides
- ☐ E. Serum uric acid
- ☐ F. Urine oxalate

**Submit**



A 23-year-old man is hospitalized with acute pancreatitis that resolves rapidly on fasting. He has suffered 2 similar episodes during the past 2 years. A gallbladder ultrasound obtained during a previous episode was normal. The patient has no other medical problems and takes no medications. He does not consume alcohol. Which of the following tests should be considered during the workup of this patient?

- ☐ A. Serum ceruloplasmin (8%)
- ☐ B. Serum cholesterol (15%)
- ☐ C. Serum ferritin (5%)
- ☒ D. Serum triglycerides (64%)
- ☐ E. Serum uric acid (2%)
- ☐ F. Urine oxalate (4%)

Correct



64%

Answered correctly



30 secs

Time Spent



02/16/2021

Last Updated

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Feedback



Suspend



End Block



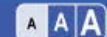
Gallstones and alcoholism are the most common causes of acute pancreatitis. Gallstones typically affect middle-aged and older patients (particularly women) unless there is a predisposing condition (eg, young patients with sickle cell disease are at increased risk for bilirubin gallstones). This young male patient does not consume alcohol and is unlikely to have gallstones, especially considering the negative results of his prior ultrasound. Thus, one of the following less common causes of acute pancreatitis likely accounts for his condition:

1. Recent endoscopic retrograde cholangiopancreatography (ERCP) procedure
2. Drugs (eg, azathioprine, sulfasalazine, furosemide, valproic acid)
3. Infections (eg, mumps, Coxsackie virus, *Mycoplasma pneumoniae*)
4. Hypertriglyceridemia
5. Structural abnormalities of the pancreatic duct (strictures, cancer, pancreas divisum) or of the ampullary region (choledochal cyst, stenosis of sphincter of Oddi)
6. Surgery (particularly of the stomach and biliary tract and after cardiac surgery)
7. Hypercalcemia

High levels of circulating triglycerides lead to increased production of free fatty acids within the pancreatic







## 7. Hypercalcemia

High levels of circulating triglycerides lead to increased production of free fatty acids within the pancreatic capillaries by pancreatic lipase. Normally, fatty acids exist in serum bound to albumin. However, if serum **triglyceride levels rise to >1000 mg/dL**, the concentration of free fatty acids exceeds the binding capacity of albumin and leads to direct injury to the pancreatic acinar cells. Thus, hypertriglyceridemia causes acute pancreatitis via direct tissue toxicity.

**(Choice A)** Decreased serum ceruloplasmin and increased hepatic copper content are diagnostic of Wilson disease. Cirrhosis, central nervous system involvement, and Kayser-Fleischer rings are characteristic findings. Wilson disease does not predispose to acute pancreatitis.

**(Choice B)** Increased serum cholesterol levels predispose to the development of systemic atherosclerosis, putting patients at increased risk for coronary artery disease, peripheral vascular disease, and stroke. In some cases, hypercholesterolemia may increase the risk of cholesterol gallstone formation, but this patient's negative gallbladder ultrasound makes this a less likely cause of his pancreatitis.

**(Choice C)** High concentrations of serum ferritin are found in hemochromatosis. Hemochromatosis can cause cirrhosis, pancreatic fibrosis and subsequent diabetes, cardiomyopathy, and secondary hypogonadism. It does not cause acute pancreatitis.





some cases, hypercholesterolemia may increase the risk of cholesterol gallstone formation, but this patient's negative gallbladder ultrasound makes this a less likely cause of his pancreatitis.

**(Choice C)** High concentrations of serum ferritin are found in hemochromatosis. Hemochromatosis can cause cirrhosis, pancreatic fibrosis and subsequent diabetes, cardiomyopathy, and secondary hypogonadism. It does not cause acute pancreatitis.

**(Choice E)** Hyperuricemia can lead to the formation of uric acid renal calculi and urate nephropathy. There is no association with acute pancreatitis.

**(Choice F)** Increased concentrations of oxalate in the urine are associated with intestinal malabsorption syndromes (eg, Crohn's disease). Calcium oxalate renal stones may form as a result. Hyperoxaluria is not associated with acute pancreatitis.

### Educational objective:

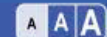
Eighty percent of acute pancreatitis cases are caused by gallstones and chronic alcoholism. Less common causes account for the other 20%. Inherited or acquired hypertriglyceridemia can cause acute pancreatitis if the serum level of triglycerides exceeds 1000 mg/dL.

Pathology

Gastrointestinal & Nutrition

Acute pancreatitis





A 36-year-old immigrant from Peru comes to the office due to difficulty swallowing liquids. He also has difficulty belching. Eating slowly and extending the neck partially relieves his symptoms. The patient has had no fever, weight loss, chest pain, cough, dyspnea, or neurologic symptoms. He has no chronic medical problems and takes no medications. He has been an active smoker for the last 18 years but does not use alcohol or illicit drugs. The patient is afebrile with normal vital signs. BMI is 24 kg/m<sup>2</sup>. On examination, the abdomen is soft, nondistended, and nontender, with no masses or organomegaly. Bowel sounds are normal. Other examination findings are unremarkable. Barium swallow shows a dilated esophagus, and manometry confirms absent peristalsis in the smooth muscle portion of the esophagus. If this patient's symptoms are caused by an infection, which of the following organisms is the most likely cause?

- ☐ A. *Candida albicans*
- ☐ B. *Clostridium botulinum*
- ☒ C. Cytomegalovirus
- ☐ D. *Helicobacter pylori*
- ☐ E. *Schistosoma mansoni*







medical problems and takes no medications. He has been an active smoker for the last 10 years but does not use alcohol or illicit drugs. The patient is afebrile with normal vital signs. BMI is 24 kg/m<sup>2</sup>. On examination, the abdomen is soft, nondistended, and nontender, with no masses or organomegaly. Bowel sounds are normal. Other examination findings are unremarkable. Barium swallow shows a dilated esophagus, and manometry confirms absent peristalsis in the smooth muscle portion of the esophagus. If this patient's symptoms are caused by an infection, which of the following organisms is the most likely cause?

- ☐ A. *Candida albicans*
- ☐ B. *Clostridium botulinum*
- ☐ C. Cytomegalovirus
- ☐ D. *Helicobacter pylori*
- ☐ E. *Schistosoma mansoni*
- ☐ F. *Trypanosoma cruzi*

**Submit**

Block Time Remaining: 00:05:07

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Feedback



Suspend



End Block



not use alcohol or illicit drugs. The patient is afebrile with normal vital signs. BMI is 24 kg/m<sup>2</sup>. On examination, the abdomen is soft, nondistended, and nontender, with no masses or organomegaly. Bowel sounds are normal. Other examination findings are unremarkable. Barium swallow shows a dilated esophagus, and manometry confirms absent peristalsis in the smooth muscle portion of the esophagus. If this patient's symptoms are caused by an infection, which of the following organisms is the most likely cause?

- ☐ A. *Candida albicans* (0%)
- ☐ B. *Clostridium botulinum* (8%)
- ☐ C. Cytomegalovirus (2%)
- ☐ D. *Helicobacter pylori* (2%)
- ☐ E. *Schistosoma mansoni* (1%)
- ✓ ☒ F. *Trypanosoma cruzi* (84%)

Correct

84%



57 secs



01/26/2021

Block Time Remaining: 00:06:00

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Feedback



Suspend



End Block



### Chagas disease

#### Epidemiology

- Caused by protozoan *Trypanosoma cruzi*
- Vector: triatomine ("kissing") bug
- Endemic in Central & South America

#### Cardiac manifestations

- Dilated cardiomyopathy with biventricular failure
- Apical wall thinning with aneurysm  $\pm$  mural thrombus
- Ventricular arrhythmias

#### Gastrointestinal manifestations

- Megaesophagus (secondary achalasia)
- Megacolon

This patient who presents with dysphagia and a dilated esophagus has **achalasia**, which is characterized by the absence of distal esophageal peristalsis and incomplete relaxation of a hypertensive lower esophageal sphincter. It is most often a primary disorder; however, in a patient from Central or South America, **secondary** achalasia due to **Chagas disease** should be suspected.

Chagas disease is caused by chronic infection with *Trypanosoma cruzi*, a slender C- or U-shaped flagellated parasite with darkly staining nucleus and kinetoplast. Parasite-related inflammation and







## manifestations

## • megacolon

This patient who presents with dysphagia and a dilated esophagus has **achalasia**, which is characterized by the absence of distal esophageal peristalsis and incomplete relaxation of a hypertensive lower esophageal sphincter. It is most often a primary disorder; however, in a patient from Central or South America, **secondary** achalasia due to **Chagas disease** should be suspected.

Chagas disease is caused by chronic infection with *Trypanosoma cruzi*, a slender C- or U-shaped flagellated parasite with darkly staining nucleus and kinetoplast. Parasitosis-related inflammation and immune-mediated cross-reactivity between the parasite and the enteric ganglia lead to destruction of the submucosal (Meissner) and myenteric (Auerbach) plexus. Denervation results in uncoordinated smooth muscle activity, increased esophageal tone, and incomplete lower esophageal relaxation. Mechanical dilation (due to obstructed liquids and solids) proximal to the functional obstruction manifests as **megaesophagus**.

Patients classically experience dysphagia progressing from solids to liquids, odynophagia (due to food impaction), difficulty belching, regurgitation, and malnutrition. Other manifestations of Chagas disease can include nonischemic **cardiomyopathy** and megacolon. In addition, patients are at higher risk for esophageal cancer.





Item 8 of 40

Question Id: 278



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



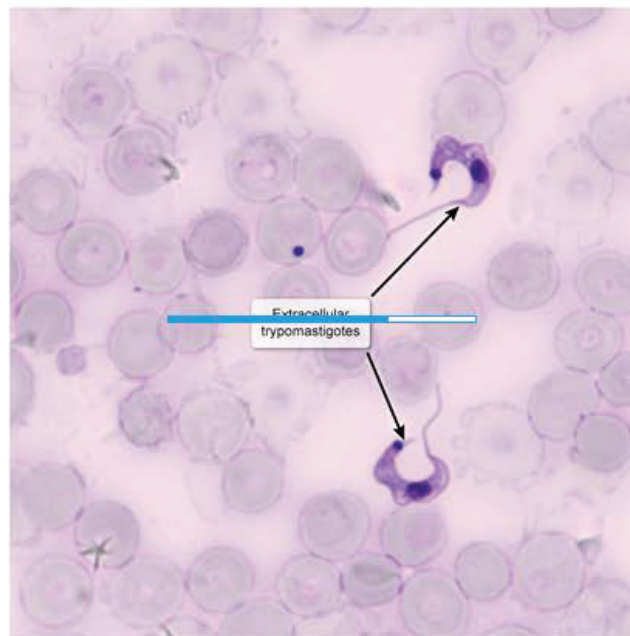
Settings

manifestations

• megacolon

### Exhibit Display

*Trypanosoma cruzi*



Extracellular  
trypomastigotes

Peripheral blood smear – Giemsa stain

©UWisc

Zoom In

Zoom Out

Reset

New | Existing

My Notebook

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Feedback



Suspend



End Block



**(Choices A and C)** Immunocompromised patients (eg, advanced HIV) can develop infectious esophagitis. *Candida albicans* causes exudative esophagitis, usually with concurrent oral thrush. Cytomegalovirus causes ulcerative esophagitis in the distal esophagus. Dysphagia and odynophagia are common with these disorders, but esophageal dilation and motility abnormalities are unexpected, and occurrence in immunocompetent patients is rare.

**(Choice B)** *Clostridium botulinum* causes botulism, a paralytic disease resulting from neurotoxins that inhibit the release of acetylcholine from presynaptic nerve terminals. Patients develop cranial nerve dysfunction and descending muscular weakness.

**(Choice D)** *Helicobacter pylori* causes gastritis and peptic ulcer. Typical manifestations include epigastric pain and nausea; however, *H pylori* does not usually cause esophageal disorders and is unlikely to cause esophageal dilation or absent peristalsis.

**(Choice E)** *Schistosoma mansoni* is a parasite found in sub-Saharan Africa, the Middle East, South America, and the Caribbean that causes intestinal or hepatic schistosomiasis; this results in gastrointestinal illness (diarrhea, abdominal pain) or portal hypertension and cirrhosis, respectively.

**Educational objective:**

Chagas disease is caused by a chronic infection by *Trypanosoma cruzi* and causes secondary esophagitis.





**(Choice B)** *Clostridium botulinum* causes botulism, a paralytic disease resulting from neurotoxins that inhibit the release of acetylcholine from presynaptic nerve terminals. Patients develop cranial nerve dysfunction and descending muscular weakness.

**(Choice D)** *Helicobacter pylori* causes gastritis and peptic ulcer. Typical manifestations include epigastric pain and nausea; however, *H pylori* does not usually cause esophageal disorders and is unlikely to cause esophageal dilation or absent peristalsis.

**(Choice E)** *Schistosoma mansoni* is a parasite found in sub-Saharan Africa, the Middle East, South America, and the Caribbean that causes intestinal or hepatic schistosomiasis; this results in gastrointestinal illness (diarrhea, abdominal pain) or portal hypertension and cirrhosis, respectively.

### Educational objective:

Chagas disease is caused by a chronic infection by *Trypanosoma cruzi* and causes secondary achalasia due to destruction of the submucosal (Meissner) and myenteric (Auerbach) plexus. Other manifestations can include nonischemic cardiomyopathy and megacolon.

Microbiology

Gastrointestinal & Nutrition

Achalasia

Subject

System

Topic

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Block Time Remaining: 00:06:00

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Feedback

Suspend

End Block



A 72-year-old man comes to the office for evaluation of constipation. His stools have been hard and pelletlike for as long as he can remember. The patient has a bowel movement every 3-4 days and frequently strains when using the bathroom. He has had associated abdominal discomfort but no hematochezia, melena, vomiting, or unexpected weight changes. The symptoms have not improved despite fiber supplementation. Vital signs are within normal limits. The abdomen is mildly distended with decreased bowel sounds. In addition to increasing water consumption, the patient is advised to try bisacodyl for constipation. What is the primary mechanism of action of this medication?

- ☐ A. Decreases surface tension of stool
- ☐ B. Draws water into the stool by creating an osmotic gradient
- ☐ C. Draws water into the stool by directly activating chloride channels
- ☐ D. Improves peristalsis by blocking mu-receptors
- ☐ E. Improves peristalsis by stimulating enteric nerves

**Submit**



A 72-year-old man comes to the office for evaluation of constipation. His stools have been hard and pelletlike for as long as he can remember. The patient has a bowel movement every 3-4 days and frequently strains when using the bathroom. He has had associated abdominal discomfort but no hematochezia, melena, vomiting, or unexpected weight changes. The symptoms have not improved despite fiber supplementation. Vital signs are within normal limits. The abdomen is mildly distended with decreased bowel sounds. In addition to increasing water consumption, the patient is advised to try **bisacodyl** for constipation. What is the primary mechanism of action of this medication?

- ☐ A. Decreases surface tension of stool (12%)
- ☐ B. Draws water into the stool by creating an osmotic gradient (40%)
- ☐ C. Draws water into the stool by directly activating chloride channels (9%)
- ☐ D. Improves peristalsis by blocking mu-receptors (10%)
- ☒ E. Improves peristalsis by stimulating enteric nerves (27%)







### Commonly used medications for constipation

**Bulk-forming laxatives**

(eg, fiber supplements)

- Binds luminal water to decrease consistency of stool
- Side effects: flatulence, abdominal distension

**Osmotic laxatives**

(eg, polyethylene glycol, magnesium hydroxide, lactulose)

- Osmotically active agent that draws water into the lumen
- Side effects: electrolyte disturbances, bloating

**Surfactant**

(eg, docusate)

- Decreases stool surface tension, enabling water to enter stool
- Side effects: rare

**Stimulant laxatives**

(eg, bisacodyl, senna)

- Activates enteric nerves in myenteric plexus to stimulate peristalsis
- Side effects: abdominal cramping, electrolyte disturbances

**Chloride channel agonist**

- Causes chloride efflux into intestinal lumen, which is



(eg, bisacodyl, senna)	disturbances
<b>Chloride channel agonist</b> (eg, lubiprostone)	<ul style="list-style-type: none"> <li>• Causes chloride efflux into intestinal lumen, which is followed by sodium and water</li> <li>• Side effects: headache, nausea</li> </ul>
<b>Peripherally acting <math>\mu</math>-opioid receptor antagonists</b> (eg, methylnaltrexone)	<ul style="list-style-type: none"> <li>• Counteracts inhibitory effect of opioids on peristalsis</li> <li>• Side effects: rare (does not cause opiate withdrawal)</li> </ul>

\*All constipation medications can cause diarrhea at high doses.

**Bisacodyl** is a **stimulant laxative** that is commonly used to treat constipation and neurogenic bowel; it is also indicated for bowel preparation prior to endoscopic procedures (eg, colonoscopy).

Bisacodyl is hydrolyzed in the colon to its active form, which directly **stimulates the enteric nerves** within the colonic myenteric plexus, thereby **increasing peristalsis** and enhancing colonic motility. It also has some minor secretory effects in the small intestine, where it increases production of cyclic AMP, indirectly increasing secretion of chloride and bicarbonate while inhibiting sodium resorption. Side effects include diarrhea, mild abdominal cramping, and electrolyte disturbances (eg, hypokalemia). Other stimulant

diarrhea, mild abdominal cramping, and electrolyte disturbances (eg, hypokalemia). Other stimulant laxatives include senna and castor oil.

**(Choice A)** Docusate reduces the surface tension of stool, enabling water and fat to enter and soften it.

**(Choice B)** Magnesium hydroxide, polyethylene glycol, and lactulose are osmotically active agents that are poorly absorbed by the intestines. These medications draw water into the intestinal lumen, thereby softening stool and making it easier to pass.

**(Choice C)** Lubiprostone is an agonist of the ClC-2 chloride channel located on the apical membrane of the intestine, which increases chloride secretion into the intestinal lumen. Sodium and water follow chloride into the lumen, resulting in increased intestinal fluid content.

**(Choice D)** Methylnaltrexone is a mu-opioid receptor antagonist designed to treat opioid-induced constipation. It does not cross the blood-brain barrier, which allows it to be used without inducing opiate-withdrawal symptoms.

### Educational objective:

Bisacodyl is a commonly used stimulant laxative that stimulates the enteric neurons within the colonic myenteric plexus, thereby increasing peristaltic activity and enhancing colonic motility.

### References

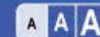




A 42-year-old man comes to the office due to increased abdominal girth associated with a 9-kg (19.8-lb) weight gain over the past month. He drinks a liter of vodka daily and denies smoking or using intravenous drugs. Blood pressure is 110/70 mm Hg. The abdomen is moderately distended, and a fluid wave is elicited. Multiple spider angiomas are present. Laboratory studies reveal thrombocytopenia, hypoalbuminemia, a normal sodium level, and an elevated PT. An upper endoscopy is performed, which shows no esophageal or gastric varices. Pharmacotherapy aimed at inhibiting which of the following should be considered for this patient?

- ☐ A. Aldosterone
- ☐ B. Alpha-adrenergic receptors
- ☐ C. Angiotensin
- ☐ D. Antidiuretic hormone
- ☐ E. Prostaglandins

**Submit**



A 42-year-old man comes to the office due to increased abdominal girth associated with a 9-kg (19.8-lb) weight gain over the past month. He drinks a liter of vodka daily and denies smoking or using intravenous drugs. Blood pressure is 110/70 mm Hg. The abdomen is moderately distended, and a fluid wave is elicited. Multiple spider angiomas are present. Laboratory studies reveal thrombocytopenia, hypoalbuminemia, a normal sodium level, and an elevated PT. An upper endoscopy is performed, which shows no esophageal or gastric varices. Pharmacotherapy aimed at inhibiting which of the following should be considered for this patient?



- ☒ A. Aldosterone (48%)
- ☐ B. Alpha-adrenergic receptors (6%)
- ☐ C. Angiotensin (14%)
- ☐ D. Antidiuretic hormone (22%)
- ☐ E. Prostaglandins (9%)





This patient with abdominal distension and a fluid wave has **ascites**. His heavy alcohol use and evidence of chronic liver disease (eg, spider angiomas, thrombocytopenia, hypoalbuminemia, elevated PT) suggest the ascites developed due to **alcoholic cirrhosis**.

In cirrhosis, portal hypertension leads to splanchnic vasodilation, which decreases the effective arterial volume and lowers the systemic blood pressure. Renal perfusion is reduced, leading to activation of the **renin-angiotensin-aldosterone system (RAAS)**, which promotes vasoconstriction (due to angiotensin) and fluid and sodium retention by the kidneys (due to aldosterone). Although this improves systemic blood pressure and renal perfusion, due to the altered hemodynamics in patients with cirrhosis (eg, elevated hydrostatic pressure due to portal hypertension, low oncotic pressure due to hypoalbuminemia) it ultimately results in third spacing of fluid with edema and ascites.

**Spirolactone**, an **aldosterone antagonist**, is used to interrupt this cycle. It induces natriuresis without blocking the critical vasoconstrictive effects of angiotensin. Spirolactone is typically used with furosemide (a loop diuretic) to increase the efficacy of natriuresis and prevent electrolyte disturbances.

**(Choices B and C)** Patients with cirrhosis have low mean arterial pressure due to splanchnic vasodilation and are dependent on the RAAS to help normalize blood pressure and renal perfusion. ACE inhibitors (eg,







lisinopril) and angiotensin receptor blockers blunt this critical response and promote organ hypoperfusion. Likewise, blockade of alpha-adrenergic receptors would cause widespread vasodilation with decreased systemic blood pressure, worsening renal perfusion and causing additional fluid accumulation.

**(Choice D)** Antidiuretic hormone (ADH) levels are increased in cirrhosis, which contributes to the development of hypervolemic hyponatremia. Although ADH inhibitors (eg, tolvapatan) have been used to treat severe hyponatremia in cirrhosis, they are not indicated in patients with normal sodium levels.

**(Choice E)** Nonsteroidal anti-inflammatory drugs inhibit prostaglandin production, which can cause renal vasoconstriction and may precipitate gastrointestinal bleeding. These medications should be avoided in patients with cirrhosis due to impaired renal perfusion at baseline and high risk of variceal bleeding.

### Educational objective:

Ascites in cirrhosis develops from hemodynamic changes related to portal hypertension. Splanchnic vasodilation decreases the systemic vascular resistance, which causes activation of the renin-angiotensin-aldosterone system and promotes vasoconstriction and sodium and water retention. Spironolactone, an aldosterone antagonist, is used to induce natriuresis and resolve ascites without blocking the critical vasoconstrictive effects of angiotensin.

### References



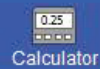
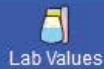


A 64-year-old woman comes to the emergency department due to intractable nausea and vomiting. She has not been able to keep anything down and feels weak and tired. The patient has had no diarrhea, constipation, or abdominal pain. She was diagnosed with breast cancer 4 weeks ago and received her first cycle of chemotherapy 1 week ago. Vital signs are within normal limits. Mucous membranes are dry. Cardiopulmonary examination is normal. Bowel sounds are normal. Which of the following agents would be most helpful in treating this patient's symptoms?

- ☐ A. Histamine H<sub>1</sub> blocker
- ☐ B. Motilin receptor agonist
- ☐ C. Mu opioid receptor agonist
- ☐ D. Muscarinic M<sub>1</sub> receptor antagonist
- ☐ E. Serotonin 5-HT<sub>3</sub> receptor antagonist

Submit





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- ☐ A. Histamine H<sub>1</sub> blocker (3%)
- ☐ B. Motilin receptor agonist (2%)
- ☐ C. Mu opioid receptor agonist (5%)
- ☐ D. Muscarinic M<sub>1</sub> receptor antagonist (6%)
- ☒ E. Serotonin 5-HT<sub>3</sub> receptor antagonist (82%)

Correct

82%  
Answered correctly

59 secs  
Time Spent

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Last Updated

Block Time Remaining: 00:08:01  
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### Characteristics of antiemetic drugs

Drug class	Examples	Clinical uses
<b>Antimuscarinics (anticholinergics)</b>	<ul style="list-style-type: none"><li>• Scopolamine</li></ul>	Motion sickness Hyperemesis gravidarum (promethazine)
<b>Antihistamines</b>	<ul style="list-style-type: none"><li>• Diphenhydramine</li><li>• Meclizine</li><li>• Promethazine</li></ul>	
<b>Dopamine receptor antagonists</b>	<ul style="list-style-type: none"><li>• Prochlorperazine</li><li>• Metoclopramide</li></ul>	Chemotherapy-induced emesis
<b>Serotonin (5-HT<sub>3</sub>) receptor antagonists</b>	<ul style="list-style-type: none"><li>• Ondansetron</li><li>• Granisetron</li></ul>	
<b>Neurokinin 1 (NK1) receptor antagonists</b>	<ul style="list-style-type: none"><li>• Aprepitant</li><li>• Fosaprepitant</li></ul>	

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The **vomiting reflex** can be activated by either humoral or neuronal stimuli. The **area postrema** in the fourth ventricle has a **chemoreceptor trigger zone** that can respond to many neurotransmitters, drugs, or toxins. The **nucleus tractus solitarius** (NTS) in the medulla receives information from the area postrema, gastrointestinal (GI) tract via the vagus nerve, vestibular system, and central nervous system (eg, meninges, hypothalamus). Neurons from the NTS project to other medullary nuclei and coordinate the vomiting process. The 5 major receptors involved in stimulating the vomiting reflex in the area postrema and adjacent vomiting center nuclei are M<sub>1</sub> muscarinic, D<sub>2</sub> dopaminergic, H<sub>1</sub> histaminic, 5-HT<sub>3</sub> serotonergic, and neurokinin 1 (NK1) receptors.

**5-HT<sub>3</sub> receptor antagonists** (eg, ondansetron, granisetron, dolasetron) are highly effective in preventing **chemotherapy-induced vomiting**. These agents act by 2 primary mechanisms: blocking **vagus**-mediated nausea and vomiting (from the GI tract stimuli) and blocking central **serotonin** receptors in the area postrema and the NTS. Other agents useful for chemotherapy-induced vomiting include NK1 **receptor antagonists** (eg, aprepitant), which inhibit substance P and help prevent both acute vomiting and delayed emesis; and dopamine receptor antagonists (eg, metoclopramide), which are associated with drowsiness and dystonic reactions.

**(Choices A and D)** Histamine blockers and antimuscarinic/anticholinergic agents are most helpful for



emesis, and dopamine receptor antagonists (eg, metoclopramide), which are associated with drowsiness and dystonic reactions.

**(Choices A and D)** Histamine blockers and antimuscarinic/anticholinergic agents are most helpful for vestibular nausea and vomiting.

**(Choice B)** Motilin regulates interdigestive migrating contractions. Erythromycin is a motilin receptor agonist used for gastroparesis.

**(Choice C)** Mu opioid receptor agonists (eg, morphine) are useful for cancer-related pain control but often have side effects such as nausea and vomiting.

### Educational objective:

Ondansetron inhibits serotonin (5-HT<sub>3</sub>) receptors and is used primarily to treat nausea and vomiting following chemotherapy. 5-HT<sub>3</sub> receptors are located peripherally in the presynaptic nerve terminals of the vagus nerve in the gastrointestinal tract. These receptors are also present centrally in the chemoreceptor trigger zone and the solitary nucleus and tract.

Pharmacology  
 Subject

Gastrointestinal & Nutrition  
 System

Nausea and vomiting  
 Topic





A 42-year-old woman comes to the office due to a 2-month history of an intermittent burning sensation in her chest with an occasional simultaneous acidic taste at the back of her throat. The symptoms occur soon after she eats a meal. The patient has no shortness of breath, lightheadedness, nausea, vomiting, or weight loss. She has no other medical conditions. The patient has smoked a pack of cigarettes daily for the last 10 years but does not use alcohol. Family history is unremarkable. Vital signs are within normal limits. BMI is 32 kg/m<sup>2</sup>. Physical examination shows no abnormalities. Urine pregnancy test is negative. Smoking cessation is discussed, and a medication is prescribed for treatment of her symptoms. The patient returns in 2 weeks for a follow-up visit and reports near-complete resolution of her symptoms. Which of the following is the most likely mechanism of action of this drug?

- ☐ A. Blockade of gastrin receptors
- ☐ B. Creation of a cytoprotective layer in the stomach
- ☐ C. Inhibition of H<sup>+</sup>/K<sup>+</sup> ATPase activity
- ☐ D. Inhibition of synthesis of gastrin
- ☐ E. Prostaglandin-mediated inhibition of acid secretion





her chest with an occasional simultaneous acidic taste at the back of her throat. The symptoms occur soon after she eats a meal. The patient has no shortness of breath, lightheadedness, nausea, vomiting, or weight loss. She has no other medical conditions. The patient has smoked a pack of cigarettes daily for the last 10 years but does not use alcohol. Family history is unremarkable. Vital signs are within normal limits. BMI is 32 kg/m<sup>2</sup>. Physical examination shows no abnormalities. Urine pregnancy test is negative. Smoking cessation is discussed, and a medication is prescribed for treatment of her symptoms. The patient returns in 2 weeks for a follow-up visit and reports near-complete resolution of her symptoms. Which of the following is the most likely mechanism of action of this drug?

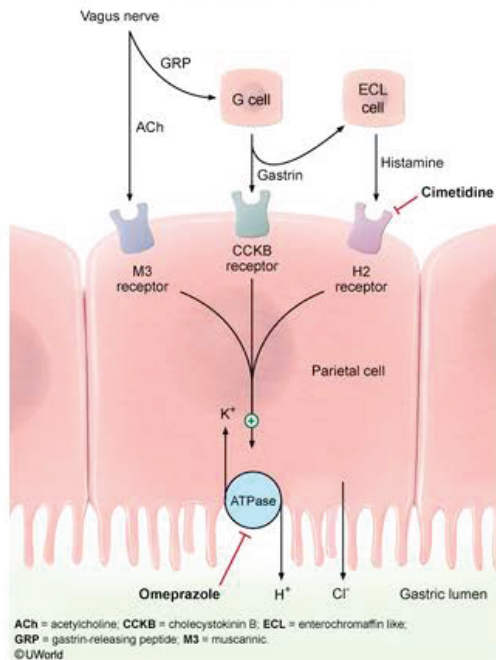
- ☐ A. Blockade of gastrin receptors (0%)
- ☐ B. Creation of a cytoprotective layer in the stomach (0%)
- ☒ C. Inhibition of H<sup>+</sup>/K<sup>+</sup> ATPase activity (95%)
- ☐ D. Inhibition of synthesis of gastrin (0%)
- ☐ E. Prostaglandin-mediated inhibition of acid secretion (1%)





## Exhibit Display

## Parietal cell acid secretion



Zoom In

Zoom Out

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This patient's heartburn is likely related to gastroesophageal reflux disease (GERD), a common disorder that occurs when gastric acid refluxes into the esophagus. Management consists of lifestyle and dietary modifications (eg, weight loss, avoidance of tobacco) as well as medications that suppress gastric acid secretion.

**Proton pump inhibitors** (PPIs) (eg, pantoprazole, omeprazole) are the most effective inhibitors of gastric acid secretion. They bind to and irreversibly **inhibit the  $H^+/K^+$  ATPase** on parietal cells. Side effects are related to elevated gastric pH and include an increased risk of *Clostridioides difficile* and nutritional deficiencies (eg, calcium, magnesium, iron).

Although less potent than PPIs, **histamine 2 receptor antagonists** (eg, famotidine, cimetidine) are also used as first-line therapy for GERD. They inhibit gastric acid secretion by targeting histamine receptors on parietal cells. These medications are less side effect-prone than PPIs; however, they have a slower onset of action, and tachyphylaxis is common.

**(Choice A)** Gastrin, a hormone released from G cells, binds to cholecystikinin (CCK) B receptors and stimulates gastric acid secretion both directly (through binding on parietal cells) and indirectly (through binding on enterochromaffin-like cells to increase histamine release). CCK receptor antagonists are not routinely used in clinical practice.





**(Choice B)** Sucralfate forms a viscous paste in the stomach, providing a cytoprotective layer that prevents the diffusion of gastric acid. It is less effective than PPIs and is typically used as an adjunctive medication for peptic ulcer disease.

**(Choice D)** Octreotide is a somatostatin analogue that inhibits gastrin synthesis (as well as many other gastrointestinal hormones). It is sometimes used in Zollinger-Ellison syndrome, but is not routinely used for GERD.

**(Choice E)** Misoprostol is a prostaglandin E1 analogue that binds prostaglandin receptors on parietal cells, reducing gastric acid production and inducing secretion of mucus and bicarbonate. Misoprostol can be used to prevent NSAID-induced gastric ulcers, but is less helpful for treating GERD; its significant uterotonic effects (eg, uterine contractions, cervical ripening) also limit its use in women of childbearing age.

### **Educational objective:**

Management of gastroesophageal reflux disease includes lifestyle and dietary modifications (eg, weight loss, tobacco avoidance) and medications such as proton pump inhibitors (PPIs) (eg, pantoprazole, omeprazole) or histamine 2 receptor antagonists (eg, ranitidine). PPIs irreversibly inhibit the  $H^+/K^+$  ATPase on parietal cells, which decreases gastric acid secretion.



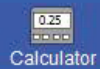


A 34-year-old man with upper gastrointestinal bleeding is brought to the local emergency department by ambulance. He was found in front of a grocery store after customers called emergency medical services. The patient is unable to provide any information, but his medical records show a history of alcoholism. After undergoing emergency evaluation and appropriate resuscitation, his condition stabilizes. Gastric lavage fluid initially contained blood but cleared quickly. Upper endoscopy shows a linear mucosal tear at the gastroesophageal junction. The process directly responsible for causing this patient's mucosal tear will most likely result in which of the following acid-base disturbances?

- ☐ A. High anion gap metabolic acidosis
- ☐ B. Metabolic alkalosis
- ☐ C. Normal anion gap metabolic acidosis
- ☐ D. Respiratory acidosis
- ☐ E. Respiratory alkalosis

**Submit**





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- ☐ A. High anion gap metabolic acidosis (15%)
- ✓ ☐ B. Metabolic alkalosis (72%)
- ✗ ☒ C. Normal anion gap metabolic acidosis (9%)
- ☐ D. Respiratory acidosis (1%)
- ☐ E. Respiratory alkalosis (1%)

Incorrect





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Characteristics of gastroesophageal mural injury

	Mallory-Weiss syndrome	Boerhaave syndrome
<b>Etiology</b>	<ul style="list-style-type: none"><li>• Forceful retching</li><li>• <b>Mucosal</b> tear</li><li>• Submucosal venous or arterial plexus bleeding</li></ul>	<ul style="list-style-type: none"><li>• Forceful retching</li><li>• <b>Transmural</b> tear</li><li>• Spillage of esophageal air/fluid into surrounding tissues</li></ul>
<b>Clinical presentation</b>	<ul style="list-style-type: none"><li>• Epigastric/back pain</li><li>• <b>Hematemesis</b> (bright red or coffee-ground)</li><li>• Possible hypovolemia</li></ul>	<ul style="list-style-type: none"><li>• Chest/back/epigastric pain</li><li>• <b>Crepitus, crunching sound</b> (Hamman sign)</li><li>• Odynophagia, dyspnea, fever, sepsis</li></ul>
<b>Studies</b>	<ul style="list-style-type: none"><li>• <b>Upper GI endoscopy</b> confirms diagnosis (&amp; can treat persistent bleeding)</li></ul>	<ul style="list-style-type: none"><li>• Chest x-ray: pneumothorax, pneumomediastinum, pleural effusion</li><li>• <b>Esophagography or CT scan with water-soluble contrast</b> confirms diagnosis</li></ul>



1



Feedback



Suspend



End Block



	<ul style="list-style-type: none"> <li>• Submucosal venous or arterial plexus bleeding</li> </ul>	<ul style="list-style-type: none"> <li>• Spillage of esophageal air/fluid into surrounding tissues</li> </ul>
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<b>Management</b>	<ul style="list-style-type: none"> <li>• Acid suppression</li> <li>• <b>Most heal spontaneously</b></li> </ul>	<ul style="list-style-type: none"> <li>• Acid suppression, antibiotics, NPO</li> <li>• <b>Emergency surgical consultation</b></li> </ul>

**GI** = gastrointestinal.

This patient has a **Mallory-Weiss tear** of the gastric mucosa near the gastroesophageal junction. Mallory-Weiss tears are caused by high intragastric pressure being transmitted to the esophagus through a tight lower esophageal sphincter. They are most commonly caused by repetitive retching and vomiting but







This patient has a **Mallory-Weiss tear** of the gastric mucosa near the gastroesophageal junction. Mallory-Weiss tears are caused by high intragastric pressure being transmitted to the esophagus through a tight lower esophageal sphincter. They are most commonly caused by repetitive **retching and vomiting** but can also occur with straining during defecation or heavy lifting, seizures, blunt abdominal injury, and upper gastrointestinal endoscopy. Repetitive vomiting leads to **metabolic alkalosis** due to net loss of acidic gastric secretions.

**(Choice A)** Unlike methanol or ethylene glycol, acute ethanol intoxication does not usually cause high anion gap metabolic acidosis, but chronic alcoholism can cause ketoacidosis in malnourished patients. Ethanol abuse is a common predisposing factor for Mallory-Weiss tears; however, it is the repetitive vomiting and retching that directly cause the tears.

**(Choice C)** Normal anion gap metabolic acidosis is usually caused by loss of bicarbonate, which can occur with prolonged diarrhea. Recurrent vomiting causes metabolic alkalosis, not acidosis.

**(Choices D and E)** Respiratory acidosis usually occurs in patients with chronic obstructive pulmonary disease or central nervous system depression (eg, narcotic overdose). Respiratory alkalosis occurs with hyperventilation (eg, panic attacks, pulmonary emboli).

**Educational objective:**





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### Educational objective:

A Mallory-Weiss tear is a tear in the gastric mucosa near the gastroesophageal junction. It typically results from repetitive forceful vomiting, which can also cause metabolic alkalosis.

### References

- [Diagnosis and management of upper gastrointestinal bleeding.](#)

Pathophysiology      Gastrointestinal & Nutrition      Mallory-weiss syndrome





A 6-hour-old boy is in the newborn nursery with feeding difficulties. The patient was born at 39 weeks gestation to a 33-year-old primigravida via cesarean delivery due to failure to progress and late decelerations seen on fetal heart tracing. Apgar scores were 8 and 9, but examination shows an infant with excessive drooling and coughing. Cardiac, respiratory, and abdominal examinations are otherwise normal at rest. When the infant attempts to breastfeed, however, several bouts of coughing and perioral cyanosis develop with oxygen saturation of 85% on room air. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Atresia of small intestine
- ☐ B. Collapse of supraglottic structures during respiration
- ☐ C. Failure of primitive foregut to separate from airway
- ☐ D. Obstruction of posterior nasal passages
- ☐ E. Thoracic herniation of abdominal viscera

**Submit**





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- ☐ A. Atresia of small intestine (2%)
- ☐ B. Collapse of supraglottic structures during respiration (5%)
- ☒ C. Failure of primitive foregut to separate from airway (83%)
- ☐ D. Obstruction of posterior nasal passages (6%)
- ☐ E. Thoracic herniation of abdominal viscera (1%)





Mark



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Next



Full Screen



Tutorial



Lab Values



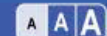
Notes



Calculator



Reverse Color



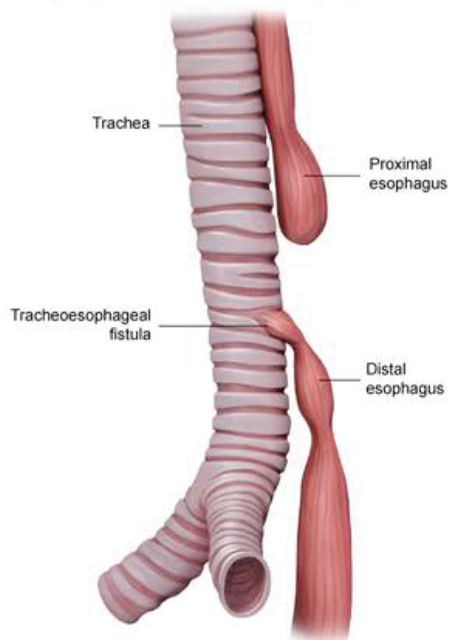
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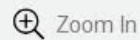
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### Exhibit Display

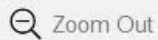
#### Esophageal atresia & tracheoesophageal fistula



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New



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My Notebook



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Feedback



Suspend



End Block



This infant's presentation is concerning for **tracheoesophageal fistula with esophageal atresia (TEF/EA)**. Normally, the trachea develops from a diverticulum that forms from the **primitive foregut**. The tracheobronchial diverticulum lengthens and separates to form the respiratory tract, while the foregut becomes the esophagus. Failure to separate most commonly leads to esophageal atresia with a remaining fistula between the trachea and esophagus.

Prenatal ultrasounds may demonstrate **polyhydramnios** due to the inability of the fetus to swallow amniotic fluid. After birth, infants typically present with significant **drooling** (due to inability to swallow saliva) and choking, **coughing**, and **cyanosis with feeds** (due to reflux of breastmilk/formula and aspiration into the trachea/lungs). The diagnosis of TEF/EA is confirmed by x-ray showing positioning of the nasogastric tube in the atretic esophageal pouch after an attempt to pass the tube into the stomach. X-ray will also show a **stomach bubble**, which results from air flow from the trachea through the fistula to the distal esophagus.

**(Choice A)** Atresia of the small intestine is a congenital defect that leads to complete obstruction of the gastrointestinal tract at the site of atresia. Neonates present with abdominal distension and bilious emesis.

**(Choice B)** Laryngomalacia presents with inspiratory stridor during infancy due to collapse of supraglottic structures during inspiration. Stridor is classically worse in the supine position and improves with upright







gastrointestinal tract at the site of atresia. Neonates present with abdominal distension and bilious emesis.

**(Choice B)** Laryngomalacia presents with inspiratory stridor during infancy due to collapse of supraglottic structures during inspiration. Stridor is classically worse in the supine position and improves with upright positioning.

**(Choice D)** **Choanal atresia** is characterized by congenital obstruction of the posterior nasal passages. Infants with bilateral choanal atresia can present with upper airway obstruction and cyanosis with feeding, but not excessive drooling and coughing. Inability to pass a nasogastric tube through the nares is suggestive of the diagnosis.

**(Choice E)** Herniation of abdominal viscera into the thoracic cavity occurs in congenital diaphragmatic hernia. Infants typically exhibit respiratory distress shortly after birth due to pulmonary hypoplasia. The presence of abdominal viscera in the thorax results in a scaphoid abdomen and bowel sounds heard over the chest.

### Educational objective:

Tracheoesophageal fistula with esophageal atresia results from failure of the primitive foregut to appropriately divide into separate trachea and esophageal structures. Infants present shortly after birth with excessive secretions and choking/cyanosis during feeds.

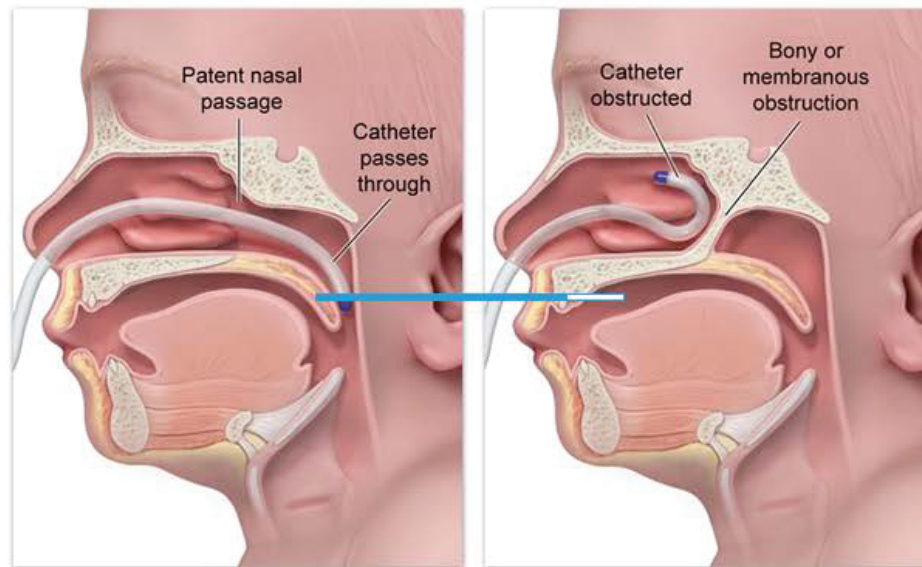




gastrointestinal tract at the site of atresia. Neonates present with abdominal distension and bilious emesis.

### Exhibit Display

#### Choanal atresia



Normal anatomy

Choanal atresia

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A 44-year-old woman comes to the office due to indigestion. The patient says she often develops right upper quadrant abdominal discomfort and nausea with fatty meals, which subside spontaneously after several hours. She does not use tobacco, alcohol, or illicit drugs. The patient immigrated to the United States from Nepal 10 years ago. Abdominal ultrasound reveals numerous gallstones, and she undergoes elective laparoscopic cholecystectomy. The stones in her gallbladder have very low cholesterol content and appear small, dark, and spiculated. Which of the following conditions most likely predisposed this patient to gallstone formation?

- ☐ A. Chronic hemolysis
- ☐ B. Metabolic syndrome
- ☐ C. Multiparity
- ☐ D. Oral contraceptive use
- ☐ E. Rapid weight loss

**Submit**





A 44-year-old woman comes to the office due to indigestion. The patient says she often develops right upper quadrant abdominal discomfort and nausea with fatty meals, which subside spontaneously after several hours. She does not use tobacco, alcohol, or illicit drugs. The patient immigrated to the United States from Nepal 10 years ago. Abdominal ultrasound reveals numerous gallstones, and she undergoes elective laparoscopic cholecystectomy. The stones in her gallbladder have very low cholesterol content and appear small, dark, and spiculated. Which of the following conditions most likely predisposed this patient to gallstone formation?

- ☒ A. Chronic hemolysis (89%)
- ☐ B. Metabolic syndrome (3%)
- ☐ C. Multiparity (2%)
- ☐ D. Oral contraceptive use (1%)
- ☐ E. Rapid weight loss (3%)





## Exhibit Display

## Pathogenesis of pigment stones

## Black stones

- Chronic hemolysis (eg, sickle cell, spherocytosis)
- ↑ Enterohepatic cycling of bilirubin (eg, ileal disease)

## Brown stones

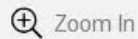
- Biliary tract infection (eg, *Escherichia coli*, liver fluke)

Release of microbial  
 $\beta$ -glucuronidases

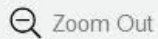
↑ Unconjugated  
bilirubin

Calcium-  
bilirubinate  
precipitation

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Calcium-





Gallstones are formed by the aggregation of bile constituents and are categorized as cholesterol stones, pigment stones, or mixed stones. **Pigment gallstones**, which account for only 10%-25% of gallstone cases in the United States, are most common in rural Asian populations. These stones can be brown to black and arise from conditions that increase the amount of **unconjugated bilirubin** in bile, which promotes calcium bilirubinate precipitation. Brown pigment stones are associated with biliary tract infections (microbes producing  $\beta$ -glucuronidases), whereas **black stones** occur in the setting of chronic **hemolysis** (eg, sickle cell anemia,  $\beta$ -thalassemia, hereditary spherocytosis) and increased enterohepatic cycling of bilirubin (eg, **ileal disease**).

Grossly, black pigment stones are usually present in significant numbers and are small, spiculated, and friable. Because these stones contain high amounts of calcium carbonates and phosphates, they are often radiopaque and appear on [x-ray](#).

**(Choices B, C, D, and E)** Obesity/metabolic syndrome, multiparity, oral contraceptive use, and rapid weight loss are significant risk factors for development of cholesterol gallstones.

### Educational objective:

Black pigment stones arise from conditions that increase the amount of unconjugated bilirubin in bile, which promotes calcium bilirubinate precipitation. This may occur in the setting of chronic hemolysis (eg, sickle







Item 15 of 40

Question Id: 69



Mark



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Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



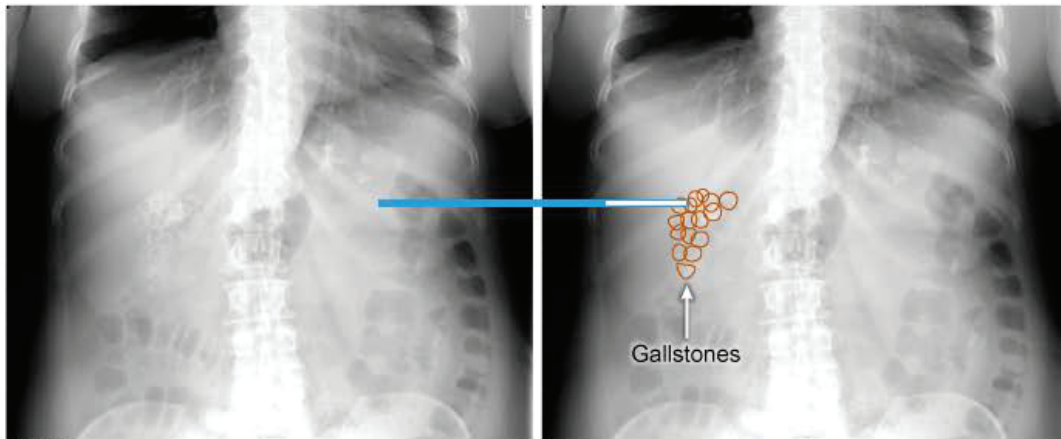
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### Exhibit Display

## Gallstones



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Suspend



End Block



promotes calcium bilirubinate precipitation. Brown pigment stones are associated with biliary tract infections (microbes producing  $\beta$ -glucuronidases), whereas **black stones** occur in the setting of chronic **hemolysis** (eg, sickle cell anemia,  $\beta$ -thalassemia, hereditary spherocytosis) and increased enterohepatic cycling of bilirubin (eg, **ileal disease**).

Grossly, black pigment stones are usually present in significant numbers and are small, spiculated, and friable. Because these stones contain high amounts of calcium carbonates and phosphates, they are often radiopaque and appear on [x-ray](#).

**(Choices B, C, D, and E)** Obesity/metabolic syndrome, multiparity, oral contraceptive use, and rapid weight loss are significant risk factors for development of cholesterol gallstones.

### Educational objective:

Black pigment stones arise from conditions that increase the amount of unconjugated bilirubin in bile, which promotes calcium bilirubinate precipitation. This may occur in the setting of chronic hemolysis (eg, sickle cell anemia,  $\beta$ -thalassemia, hereditary spherocytosis) and increased enterohepatic cycling of bilirubin (eg, ileal disease).

### References

- [New pathophysiological concepts underlying pathogenesis of pigment gallstones.](#)





A previously healthy 4-year-old girl is brought to the office because her parents noticed dark red blood on her toilet tissue. She has no abdominal pain or discomfort with stooling. Her temperature is 36.7 C (98 F), blood pressure is 100/40 mm Hg, and pulse is 112/min. Physical examination shows a soft and nontender abdomen, and bowel sounds are present. Her hemoglobin is 8 g/dL and platelet count is 215,000/mm<sup>3</sup>. Coagulation profile is normal. Sequential imaging using <sup>99m</sup>Tc-pertechnetate scintigraphy demonstrates focal radiotracer accumulation in the right lower quadrant. Which of the following embryologic processes most likely failed in this patient?

- ☐ A. Ascent of the kidneys into the abdomen
- ☐ B. Closure of lateral body folds at the umbilicus
- ☒ C. Hindgut descent along the inferior mesenteric artery
- ☐ D. Midgut rotation around the superior mesenteric artery
- ☐ E. Neural crest cell migration into the bowel wall
- ☐ F. Obliteration of the omphalomesenteric (vitelline) duct







her toilet tissue. She has no abdominal pain or discomfort with stooling. Her temperature is 36.7 C (98 F), blood pressure is 100/40 mm Hg, and pulse is 112/min. Physical examination shows a soft and nontender abdomen, and bowel sounds are present. Her hemoglobin is 8 g/dL and platelet count is 215,000/mm<sup>3</sup>. Coagulation profile is normal. Sequential imaging using <sup>99m</sup>Tc-pertechnetate scintigraphy demonstrates focal radiotracer accumulation in the right lower quadrant. Which of the following embryologic processes most likely failed in this patient?

- ☐ A. Ascent of the kidneys into the abdomen (4%)
- ☐ B. Closure of lateral body folds at the umbilicus (1%)
- ☐ C. Hindgut descent along the inferior mesenteric artery (6%)
- ☒ D. Midgut rotation around the superior mesenteric artery (13%)
- ☐ E. Neural crest cell migration into the bowel wall (6%)
- ☒ F. Obliteration of the omphalomesenteric (vitelline) duct (66%)

Incorrect

Correct answer



66%

Answered correctly



01 min, 30 secs

Time spent



09/09/2020

Last updated

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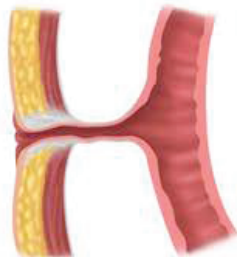


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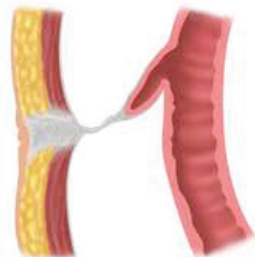


## Exhibit Display

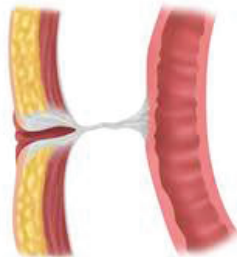
## Vitelline duct abnormalities



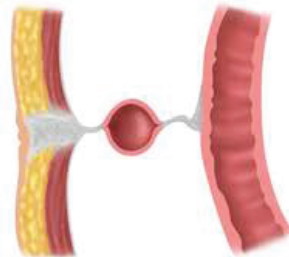
Persistent vitelline duct



Meckel diverticulum

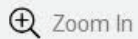


Vitelline sinus



Vitelline duct cyst (enterocyst)

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**Meckel diverticulum** is an ileal outgrowth that results from failed obliteration of the vitelline (omphalomesenteric) duct. When patients are symptomatic, the most common manifestation of Meckel diverticulum is spontaneous but **painless** lower gastrointestinal (GI) **bleeding**. Meckel diverticulum is also a potential lead point for intussusception, which can present with colicky abdominal pain and "**currant jelly**" (strawberry jam appearance) stools.

Ectopic gastric mucosa in the Meckel diverticulum secretes acid and causes local ulceration and bleeding. The radioisotope  $^{99m}\text{Tc}$ -pertechnetate has an affinity for **parietal cells** of the gastric mucosa (including ectopic sites) and is used in a nuclear medicine procedure called the  $^{99m}\text{Tc}$ -pertechnetate scan. Increased uptake of  $^{99m}\text{Tc}$ -pertechnetate in the periumbilical/right lower quadrant (RLQ) is characteristic of Meckel diverticulum.

**(Choice A)** If the lower poles of the kidney fuse, a horseshoe kidney forms and is unable to ascend past the inferior mesenteric artery from the pelvis to the abdomen. Some patients may have hematuria but most are asymptomatic.

**(Choice B)** The midgut normally herniates into the yolk sac during the 6th week of gestation and returns to the abdominal cavity in the 10th week. If lateral body folds do not develop and close, abdominal contents

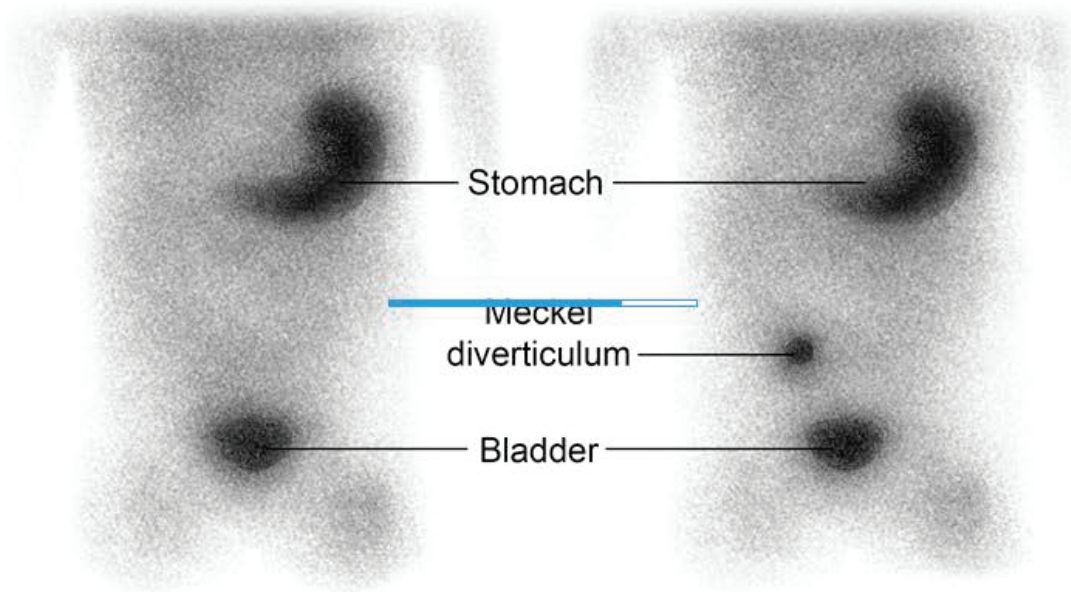






## Exhibit Display

## Meckel scan



Normal

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are asymptomatic.

**(Choice B)** The midgut normally herniates into the yolk sac during the 6th week of gestation and returns to the abdominal cavity in the 10th week. If lateral body folds do not develop and close, abdominal contents herniate through the **ventral wall defect**. Omphalocele and gastroschisis do not commonly present with GI bleeding.

**(Choice C)** The hindgut gives rise to the distal third of the transverse colon, descending and sigmoid colon, rectum, and upper part of the anal canal. Failure of proper descent during development can lead to imperforate anus, which does not bleed.

**(Choice D)** Abnormal midgut rotation around the superior mesenteric artery leads to intestinal malrotation. The intestine is fixed by fibrous adhesive bands and can cause obstruction and painful bilious emesis in the newborn.

**(Choice E)** Neural crest cells migrate in a craniocaudal direction to the internal anal sphincter. If this process fails, then the myenteric plexus does not form, and the aganglionic sigmoid colon/rectum segments become inactive and narrow. **Hirschsprung disease** manifests as intestinal obstruction in the neonate and presents with delayed passage of meconium, bilious vomiting, and abdominal distension.

**Educational objective:**





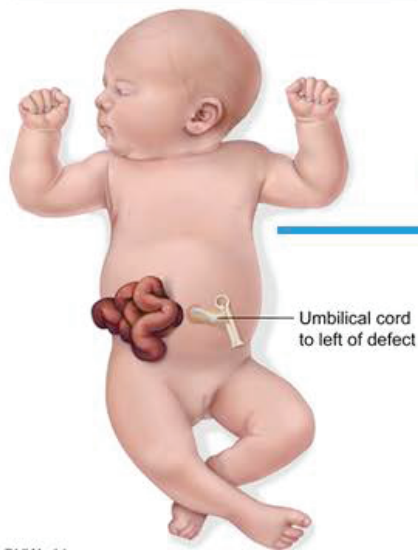
are asymptomatic.

### Exhibit Display

#### Gastroschisis vs. omphalocele

##### Gastroschisis

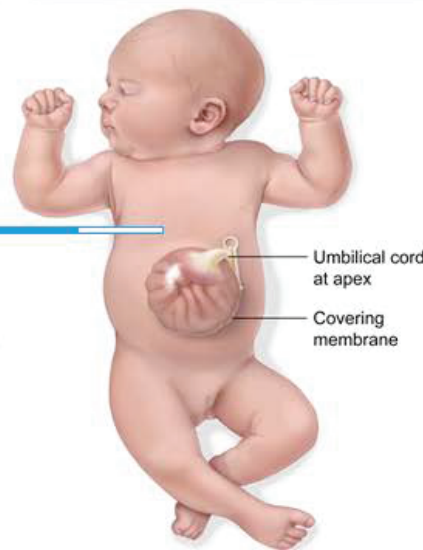
Eviscerated bowel with no covering membrane



Umbilical cord  
to left of defect

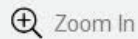
##### Omphalocele

Sac containing multiple organs

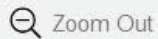


Umbilical cord  
at apex  
Covering  
membrane

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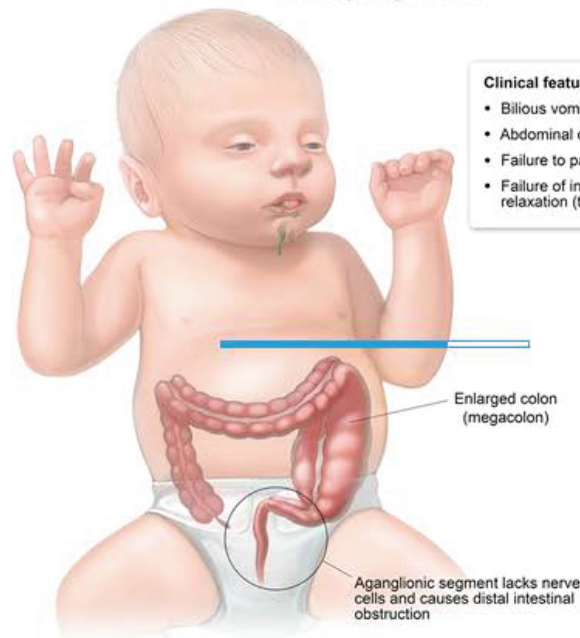




are asymptomatic.

### Exhibit Display

#### Hirschsprung disease



##### Clinical features

- Bilious vomiting
- Abdominal distension
- Failure to pass meconium
- Failure of internal anal sphincter relaxation (tight anal sphincter)

Enlarged colon  
(megacolon)

Aganglionic segment lacks nerve  
cells and causes distal intestinal  
obstruction

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Zoom In

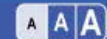
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colon, rectum, and upper part of the anal canal. Failure of proper descent during development can lead to imperforate anus, which does not bleed.

**(Choice D)** Abnormal midgut rotation around the superior mesenteric artery leads to intestinal malrotation. The intestine is fixed by fibrous adhesive bands and can cause obstruction and painful bilious emesis in the newborn.

**(Choice E)** Neural crest cells migrate in a craniocaudal direction to the internal anal sphincter. If this process fails, then the myenteric plexus does not form, and the aganglionic sigmoid colon/rectum segments become inactive and narrow. [Hirschsprung disease](#) manifests as intestinal obstruction in the neonate and presents with delayed passage of meconium, bilious vomiting, and abdominal distension.

### Educational objective:

Meckel diverticulum results from failed obliteration of the vitelline (omphalomesenteric) duct and usually presents with spontaneous but painless lower gastrointestinal bleeding.  $^{99m}\text{Tc}$ -pertechnetate localizes ectopic gastric mucosa, and its increased uptake is diagnostic for Meckel diverticulum.

### References

- [Clinical Features of Symptomatic Meckel's Diverticulum in Children: Comparison of Scintigraphic and Non-scintigraphic Diagnosis](#)





A 43-year-old man comes to the office with a several-month history of fatigue, rash, flushing, and abdominal cramps. His rash is worse with rubbing or scratching, and he has diffuse itching after hot showers. The patient is frequently dizzy and light-headed after prolonged standing and had an episode of syncope while working in the hot sun. He used to be healthy and physically active but has had to reduce his normal activity. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. Skin examination shows a maculopapular rash. Skin biopsy shows large clusters of mast cells that are positive for KIT (CD 117). Which of the following additional findings are most likely present in this patient?

- ☐ A. Bacterial colonization of the stomach
- ☐ B. Gastric atrophy
- ☐ C. Gastric hypersecretion
- ☐ D. Gastric hypomotility
- ☐ E. Pancreatic endocrine tumor
- ☐ F. Pernicious anemia







abdominal **cramps**. His rash is worse with rubbing or scratching, and he has diffuse itching after hot showers. The patient is frequently dizzy and light-headed after prolonged standing and had an episode of syncope while working in the hot sun. He used to be healthy and physically active but has had to reduce his normal activity. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. Skin examination shows a maculopapular rash. Skin biopsy shows large clusters of mast cells that are positive for KIT (CD 117). Which of the following additional findings are most likely present in this patient?

- ☐ A. Bacterial colonization of the stomach (3%)
- ☐ B. Gastric atrophy (8%)
- ☒ C. Gastric hypersecretion (32%)
- ☐ D. Gastric hypomotility (8%)
- ☒ E. Pancreatic endocrine tumor (33%)
- ☐ F. Pernicious anemia (14%)

**Incorrect**

Correct answer



32%

Answered correctly



01 min, 27 secs

Time spent



01/25/2021

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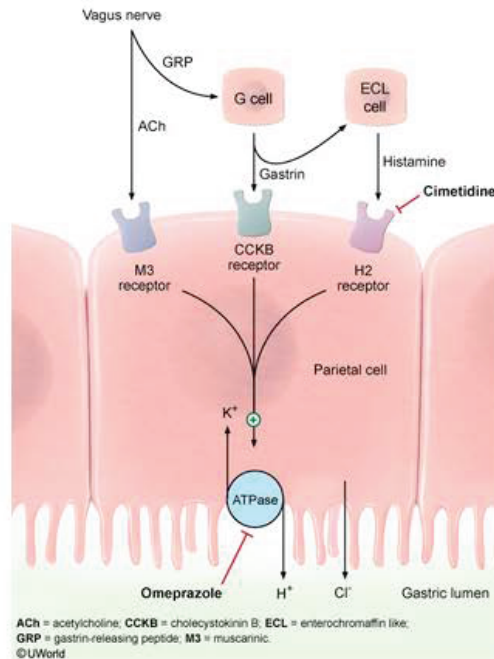
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## Exhibit Display

## Parietal cell acid secretion



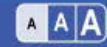
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GRP = gastrin-releasing peptide; M3 = muscarinic.  
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**Gastric acid** secretion by parietal cells in the fundus and body of the stomach is stimulated by:

1. **Histamine** binds  $H_2$  receptors and increases intracellular cyclic AMP (cAMP) concentration.
2. **Acetylcholine** binds  $M_3$  muscarinic receptors and leads to an increase in intracellular calcium.
3. **Gastrin** binds to the cholecystikinin B receptor and increases the intracellular calcium concentration.

It also stimulates histamine synthesis and release by enterochromaffin-like cells in the stomach.

Intracellular calcium and cAMP activate protein kinases and lead to increased transport of  $H^+$  by  $H^+/K^+$  ATPase into the gastric lumen.

In **systemic mastocytosis**, clonal mast cell proliferation occurs in the bone marrow, skin, and other organs. Mast cell proliferation often is associated with mutations in the **KIT** receptor tyrosine kinase. These cells are characterized by prominent expression of mast cell tryptase. Excessive **histamine** release from degranulation of mast cells mediates many of the symptoms of the disease, such as syncope, flushing, hypotension, pruritus, and urticaria. In addition, histamine induces gastric acid secretion, which can lead to gastric ulceration. The excess acid also inactivates pancreatic and intestinal enzymes, causing diarrhea. Other gastrointestinal symptoms include nausea, vomiting, and abdominal cramps.

(Choices A, B, and E) Gastric mucosal atrophy often results from colonization with *Helicobacter pylori*. It







**(Choices A, B, and F)** Gastric mucosal atrophy often results from colonization with *Helicobacter pylori*. It can also be caused by autoimmune gastritis, which may lead to pernicious anemia due to loss of intrinsic factor from parietal cells. Symptoms of atrophic gastritis may include nausea, indigestion, and epigastric discomfort, but this patient's skin symptoms are more consistent with mastocytosis.

**(Choice D)** Gastric hypomotility (gastroparesis) occurs with diabetes mellitus, uremia, hypothyroidism, and other metabolic disorders. Gastroparesis causes constipation, early satiety, and food stasis with vomiting.

**(Choice E)** Pancreatic endocrine tumors may secrete gastrin (Zollinger-Ellison syndrome), insulin (hypoglycemia), glucagon (hyperglycemia, rash), somatostatin (diarrhea, cholelithiasis, hyperglycemia), or vasoactive intestinal peptide (watery diarrhea, hypokalemia, achlorhydria). These disorders would not be associated with excess mast cells in the skin.

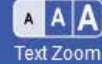
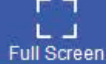
### Educational objective:

Systemic mastocytosis is characterized by the abnormal proliferation of mast cells and increased histamine release. Histamine causes hypersecretion of gastric acid by parietal cells in the stomach as well as a variety of other symptoms (eg, hypotension, flushing, pruritus).

### References

- [Mastocytosis](#).





A 27-year-old woman, gravida 1 para 0, with gestational diabetes mellitus comes to the hospital at 38 weeks gestation for evaluation of abdominal pain. The patient is scheduled for an elective cesarean section at 39 weeks as a recent ultrasound revealed that the estimated fetal weight is 5200 g (11 lb 4 oz). Examination reveals that the patient is in active labor and the fetus is in breech presentation; an urgent cesarean section is performed. During the surgery, the rectus abdominis muscle is split vertically, but space appears to be limited. In anticipation of a large-for-gestational-age baby, a decision is made to transect the rectus abdominis muscle. If the rectus abdominis muscle is incised laterally, which of the following structures is at greatest risk of injury?

- ☐ A. Deep circumflex iliac artery
- ☐ B. Deep inguinal ring
- ☐ C. Femoral sheath
- ☐ D. Inferior epigastric artery
- ☐ E. Lateral femoral cutaneous nerve
- ☐ F. Superior epigastric artery





weeks gestation for evaluation of abdominal pain. The patient is scheduled for an elective cesarean section at 39 weeks as a recent ultrasound revealed that the estimated fetal weight is 5200 g (11 lb 4 oz). Examination reveals that the patient is in active labor and the fetus is in breech presentation; an urgent cesarean section is performed. During the surgery, the rectus abdominis muscle is split vertically, but space appears to be limited. In anticipation of a large-for-gestational-age baby, a decision is made to transect the rectus abdominis muscle. If the rectus abdominis muscle is incised laterally, which of the following structures is at greatest risk of injury?

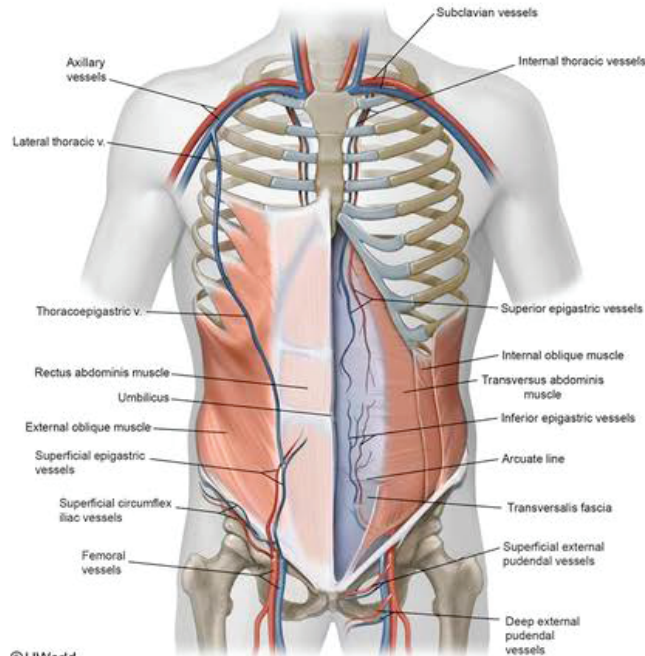
- ☐ A. ~~Deep circumflex iliac artery~~ (1%)
- ☐ B. ~~Deep inguinal ring~~ (4%)
- ☐ C. ~~Femoral sheath~~ (4%)
- ☒ D. Inferior epigastric artery (73%)
- ☐ E. Lateral femoral cutaneous nerve (4%)
- ☐ F. ~~Superior epigastric artery~~ (11%)





### Exhibit Display

#### Vessels of the abdominal wall



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Rectus abdominis muscle



The rectus abdominis is a pair of vertically aligned muscles that connect the xiphoid process to the pubic symphysis. The **arcuate line** is a horizontal line located below the umbilicus that demarcates the lower limit of the posterior rectus sheath. Above the arcuate line, the rectus abdominis is surrounded by anterior and posterior sheaths; below, the muscle is covered only by the anterior sheath.

The superior (**Choice F**) and inferior epigastric arteries supply the superior and inferior portions of the rectus abdominis muscle, respectively. The epigastric artery ascends the posterior surface of the rectus abdominis muscle and enters the lateral aspect of this muscle at the arcuate line. Because there is **no supporting posterior sheath**, trauma to the **inferior epigastric artery** below the arcuate line can result in significant hemorrhage.

Regardless of the direction of skin incision, a **cesarean delivery** typically involves midline vertical separation of the rectus abdominis muscle. **Horizontal transection** of the **rectus abdominis** muscle may be considered when additional space is necessary (eg, due to fetal weight or position). If the **rectus abdominis** is **transected horizontally**, the **inferior epigastric arteries** must be identified and ligated bilaterally to prevent bleeding complications (eg, hematoma).

(**Choice A**) The deep circumflex iliac artery supplies blood to the anterior iliac crest and arises from the lateral aspect of the external iliac artery. It is located significantly laterally and inferiorly to the rectus





**(Choice A)** The deep circumflex iliac artery supplies blood to the anterior iliac crest and arises from the lateral aspect of the external iliac artery. It is located significantly laterally and inferiorly to the rectus abdominis muscle.

**(Choice B)** The inguinal canal contains structures (eg, ilioinguinal nerve, round ligament [women], spermatic cord [men]) between the abdomen and external genitalia. Men are more susceptible to [inguinal hernias](#) compared to women due to their relatively larger deep inguinal ring.

**(Choice C)** The femoral sheath is located in the inguinofemoral region and contains the [femoral artery](#), femoral vein, and femoral canal.

**(Choice E)** The [lateral femoral cutaneous nerve](#) travels under the inguinal ligament. It provides sensory innervation to the anterolateral thigh. Entrapment (meralgia paresthetica) most commonly occurs in obese or pregnant persons or in those who wear garments that are tight around the hip.

**Educational objective:**

Horizontal transection of the rectus abdominis muscle must be performed with great caution as the inferior epigastric arteries enter this muscle at the level of the arcuate line. The inferior epigastric arteries below the arcuate line are susceptible to injury (eg, hematoma) due to lack of a supporting posterior rectus







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Previous

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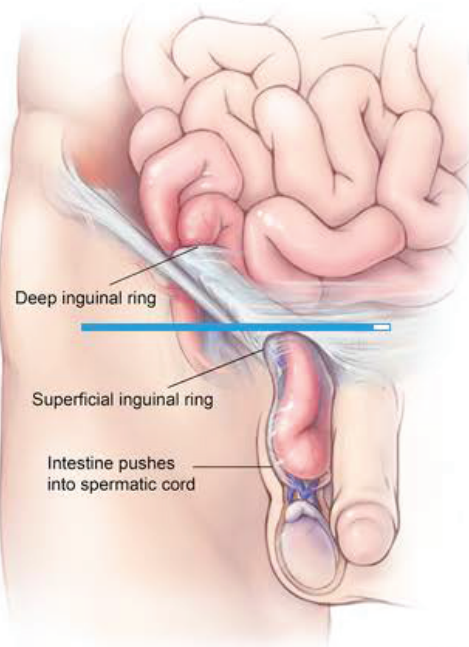
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## Exhibit Display

## Indirect inguinal hernia



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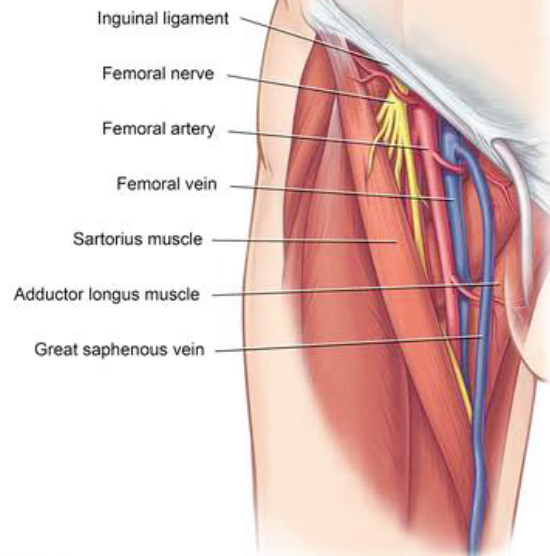
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## Exhibit Display

## Femoral triangle



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Next

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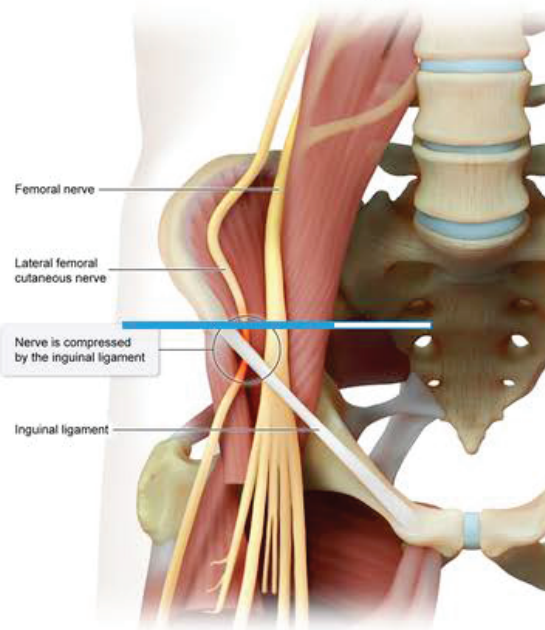
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## Exhibit Display

## Lateral femoral cutaneous nerve &amp; meralgia paresthetica



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Previous



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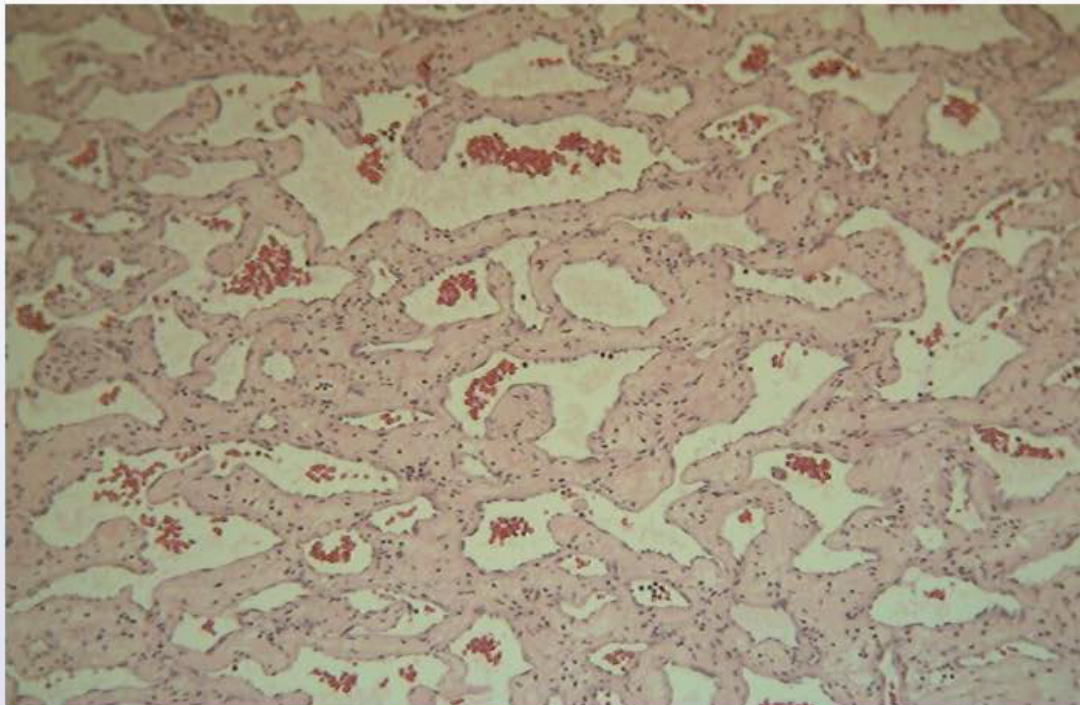


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A mass resected from the liver of a 32-year-old woman has the morphology demonstrated on the slide below.



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Previous



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Tutorial



Lab Values



Notes



Calculator



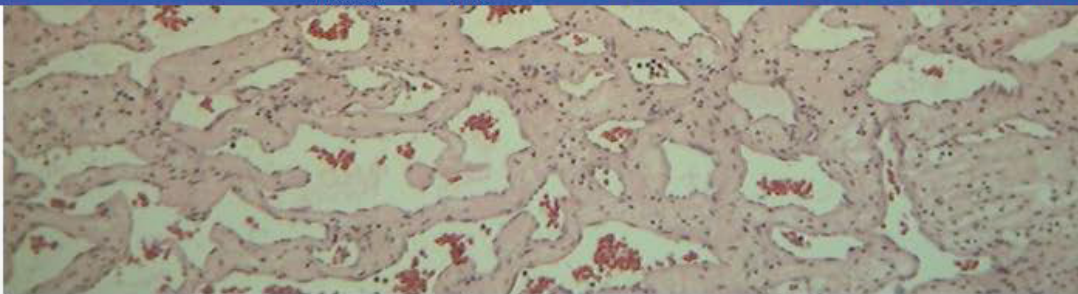
Reverse Color



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Which of the following is the most accurate statement concerning this patient's condition?

- ☐ A. Malignant transformation is a rule
- ☐ B. It is the most common benign liver tumor
- ☐ C. It can regress upon oral contraceptive discontinuation
- ☒ D. It is strongly associated with hemochromatosis
- ☐ E. Biopsy is indicated to confirm the diagnosis

**Submit**

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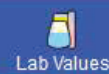
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Full Screen



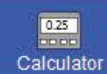
Tutorial



Lab Values



Notes



Calculator



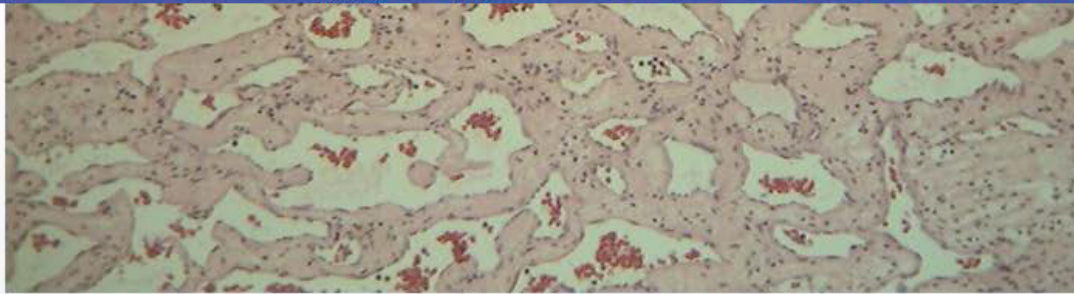
Reverse Color



Text Zoom



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Which of the following is the most accurate statement concerning this patient's condition?

- ☐ A. Malignant transformation is a rule (5%)
- ☒ B. It is the most common benign liver tumor (35%)
- ☐ C. It can regress upon oral contraceptive discontinuation (32%)
- ☐ D. It is strongly associated with hemochromatosis (16%)
- ☐ E. Biopsy is indicated to confirm the diagnosis (10%)

Correct



35%

Answered correctly



15 secs

Time spent



09/30/2020

Last updated

Block Time Remaining: 00:16:45

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



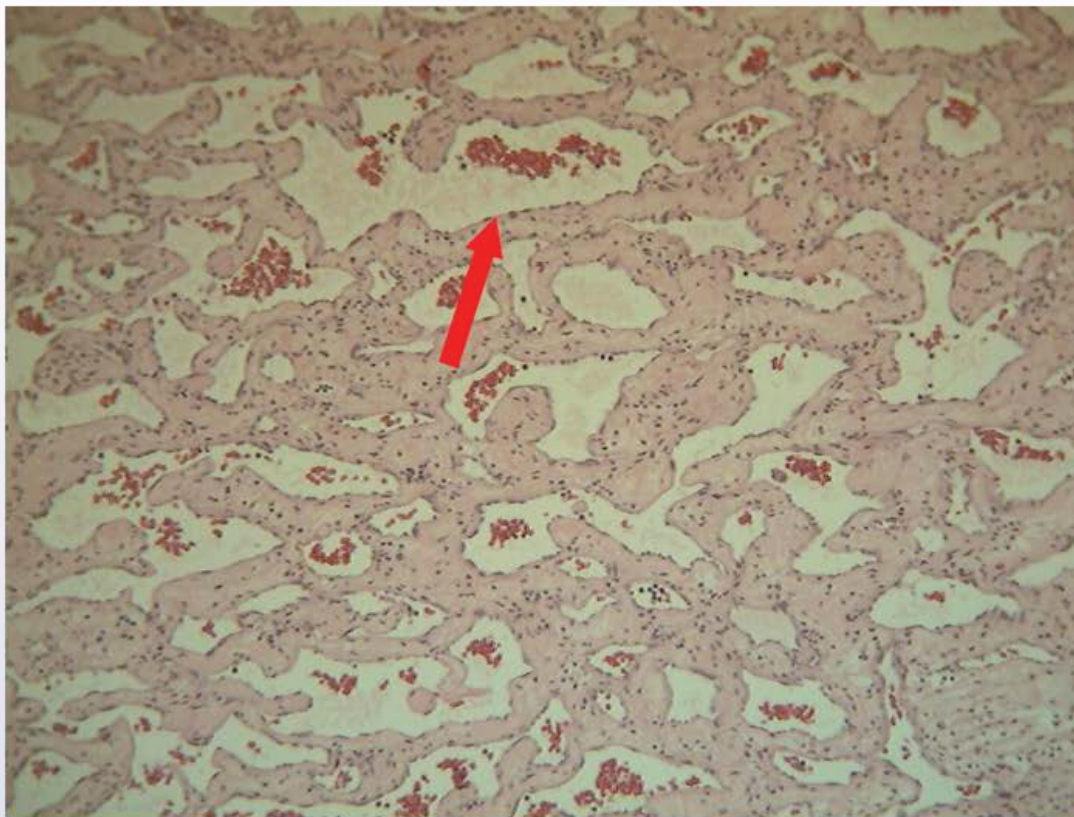
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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

Cavernous hemangioma is the most common benign liver tumor, typically presenting in adults 30-50 years of age. These benign tumors are thought to be congenital malformations that enlarge by ectasia, not hyperplasia or hypertrophy. Hemangiomas may occur singly or in multiples and are well-circumscribed masses of spongy consistency, typically measuring less than 5 cm in width. Microscopically, these tumors consist of cavernous, blood-filled vascular spaces of variable size lined by a single epithelial layer (arrow). Collagenous scars or fibrous nodules may be seen in association with thrombosis. Most patients are asymptomatic, although some will complain of abdominal pain and right upper quadrant fullness. Prognosis is usually excellent, with surgical resection an option for those patients who are symptomatic or who have compression of adjacent structures.

**(Choice A)** On rare occasion, giant hemangiomas are found to be malignant vascular tumors. The vast majority of hemangiomas are benign lesions, however.

**(Choice C)** Hepatic adenomas can regress with the discontinuation of oral contraceptives, but hemangiomas are not similarly affected.

**(Choice D)** Hepatocellular carcinoma (not hemangioma) can be associated with hemochromatosis.

**(Choice E)** Biopsy of a suspected hemangioma is not advisable, as the procedure has been known to



Feedback



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Previous



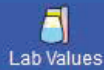
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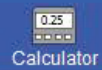
Tutorial



Lab Values



Notes



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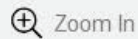
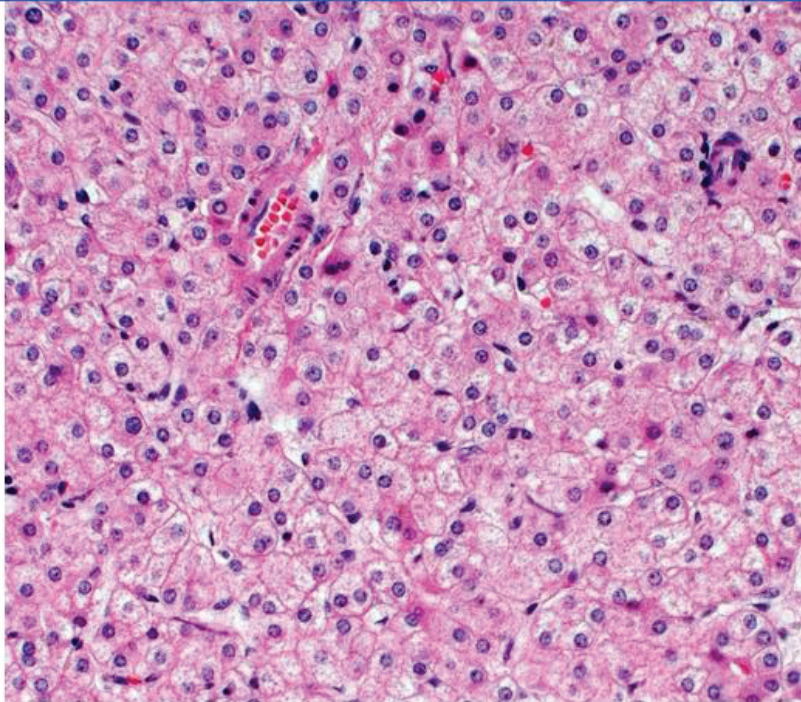


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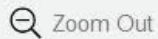


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Zoom In



Zoom Out



Reset



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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

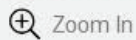
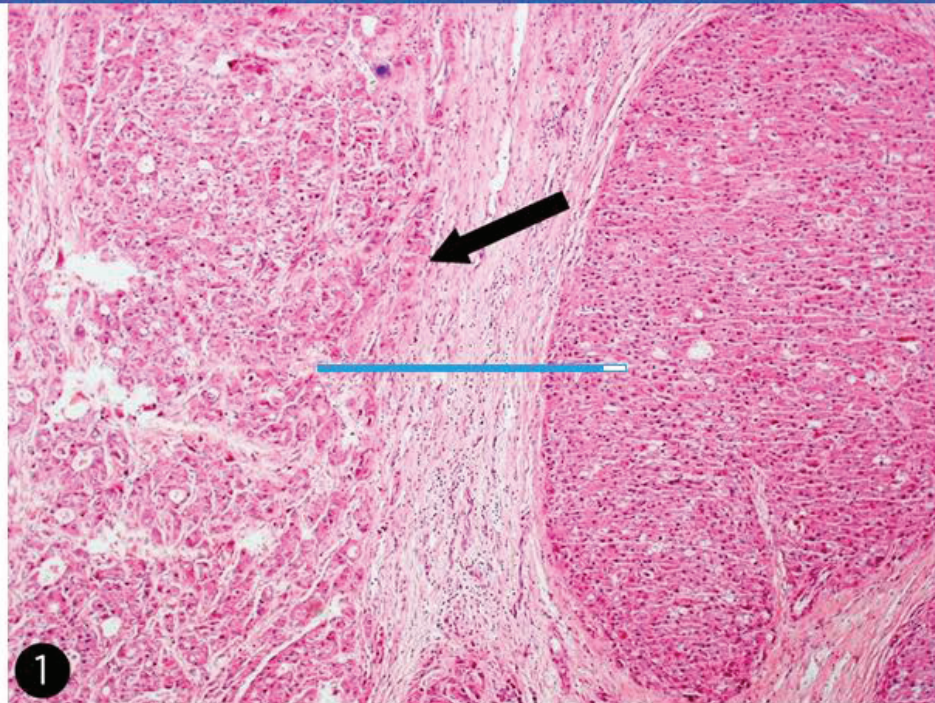


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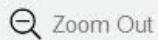


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## Exhibit Display



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** On rare occasion, giant hemangiomas are found to be malignant vascular tumors. The vast majority of hemangiomas are benign lesions, however.

**(Choice C)** **Hepatic adenomas** can regress with the discontinuation of oral contraceptives, but hemangiomas are not similarly affected.

**(Choice D)** **Hepatocellular carcinoma** (not hemangioma) can be associated with hemochromatosis.

**(Choice E)** Biopsy of a suspected hemangioma is not advisable, as the procedure has been known to cause fatal hemorrhage and is of low diagnostic yield.

### Educational objective:

Cavernous hemangioma is the most common benign liver tumor. Microscopically, these tumors consist of cavernous, blood-filled vascular spaces of variable size lined by a single epithelial layer. The biopsy of a suspected hemangioma is not advisable, as the procedure has been known to cause fatal hemorrhage and is of low diagnostic yield.

Pathology

Gastrointestinal &amp; Nutrition

Hemangioma

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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Settings

A 65-year-old woman has had several months of progressive fatigue, diminished appetite, and unintentional weight loss. The patient has no chronic medical conditions. She has not received medical care in many years and has not had recommended cancer screening. The patient suddenly dies while undergoing evaluation. Autopsy reveals abnormal liver findings, as shown in the exhibit below.



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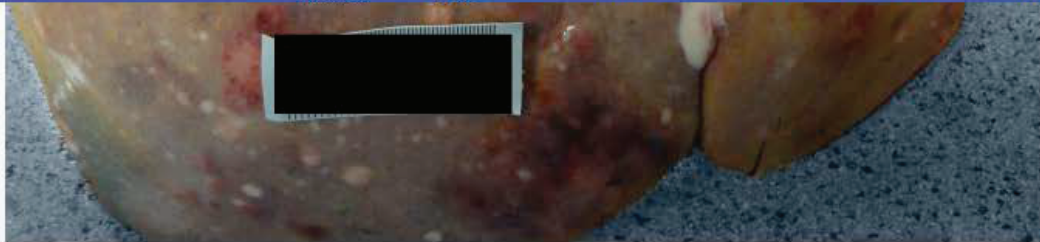


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Microscopic evaluation of the lesions reveals neoplastic cells. Which of the following is the most likely cause of this patient's liver lesions?

- ☐ A. Lymphatic spread of a malignancy
- ☐ B. Malignancy metastasizing via the hepatic veins
- ☐ C. Malignancy spreading through the portal circulation
- ☐ D. Primary neoplastic transformation of hepatocytes
- ☐ E. Transcoelomic spread of a malignancy

Submit



Microscopic evaluation of the lesions reveals neoplastic cells. Which of the following is the most likely cause of this patient's liver lesions?

- ☐ A. Lymphatic spread of a malignancy (11%)
- ☐ B. Malignancy metastasizing via the hepatic veins (12%)
- ☒ C. Malignancy spreading through the portal circulation (67%)
- ☐ D. Primary neoplastic transformation of hepatocytes (4%)
- ☐ E. Transcoelomic spread of a malignancy (4%)

Correct

67%



21 secs



02/11/2021



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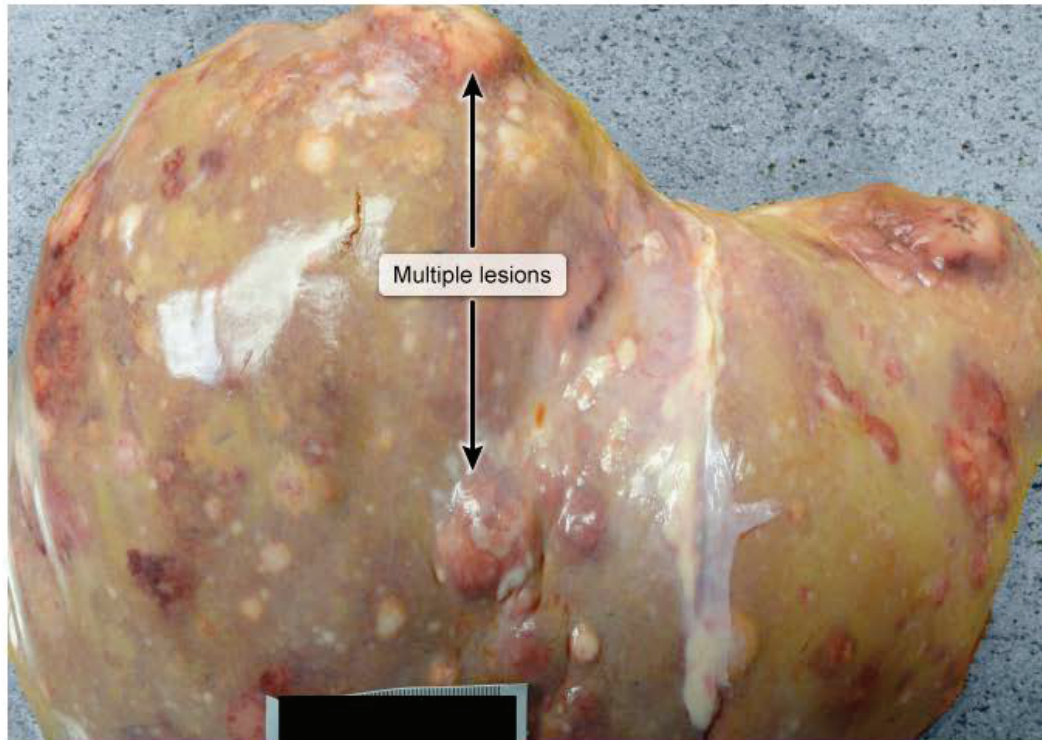


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### Metastatic colorectal carcinoma to liver





Liver neoplasms are most often due to **metastases** from distant tumors rather than primary liver cancer (eg, hepatocellular carcinoma). Metastatic disease to the liver is particularly likely when **multiple tumors** are present (as seen in this case) and there is no history of underlying hepatic disease such as alcoholic cirrhosis or hepatitis C. The liver is vulnerable to the metastatic spread of cancer due to the following anatomic considerations:

- The presence of **fenestrated hepatic sinusoidal epithelium**, which allows tumor cells to easily pass from the bloodstream through to the parenchyma.
- **Dual blood supply** from the portal and systemic circulation, which increases the likelihood of circulating tumor cells depositing in the liver.

The most common cause of liver metastases is **colorectal cancer**, which spreads directly from the colon or superior rectum through the **portal venous system** to the liver. This patient, who has not received recommended cancer screening (eg, colonoscopy), likely developed hepatic metastases from colorectal cancer. Gastric and pancreatic cancers also frequently spread through the portal system to the liver.

**(Choice A)** Lymphatic spread of tumor cells is a common mechanism of metastases, but it is not the primary source of most metastatic liver lesions.



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

primary source of most metastatic liver lesions.

**(Choice B)** Tumors (eg, breast, lung, melanoma) can spread to the liver through the systemic circulation via the hepatic artery (rather than the portal circulation). The hepatic vein drains out of the liver; it does not bring blood into the liver.

**(Choice D)** Primary hepatic cancer is thirtyfold less common than metastatic disease. Most primary lesions are solitary tumors and arise in individuals with underlying liver disease. This patient, who did not have recommended cancer screening (eg, colonoscopy) and has multiple liver tumors, most likely has metastatic disease.

**(Choice E)** Although gastrointestinal cancers can spread to the peritoneum and then invade the liver, this is much less common than hematogenous dissemination through the portal system. Metastasis through the peritoneal space most commonly occurs with ovarian cancer and gastric (Krukenberg) tumors.

### Educational objective:

Most hepatic neoplasms are due to metastatic disease from a distant site. Colorectal cancer is the most common cause of hepatic metastases due to direct blood flow from the colon (and superior rectum) to the liver via the portal venous circulation.

Pathology      Gastrointestinal & Nutrition      Colorectal polyps and cancer

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Feedback



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End Block

A 54-year-old man comes to the office with abdominal pain, chronic diarrhea, and recent weight loss. He has had episodic abdominal pain in the past, but lately it has become persistent and worsens after eating. The patient does not use tobacco or illicit drugs but does consume alcohol regularly. An upright abdominal x-ray reveals calcifications in the epigastric area. Which of the following is the most likely cause of his diarrhea?

- ☐ A. Bile salt malabsorption
- ☐ B. Digestive enzyme deficiency
- ☐ C. Elevated portal venous pressure
- ☐ D. Excessive gastrin production
- ☐ E. Immune-mediated enteropathy
- ☐ F. Nutrient absorption interference by alcohol


**Submit**



A 54-year-old man comes to the office with abdominal pain, chronic diarrhea, and recent weight loss. He has had episodic abdominal pain in the past, but lately it has become persistent and worsens after eating. The patient does not use tobacco or illicit drugs but does consume alcohol regularly. An upright abdominal x-ray reveals **calcifications** in the **epigastric area**. Which of the following is the most likely cause of his diarrhea?

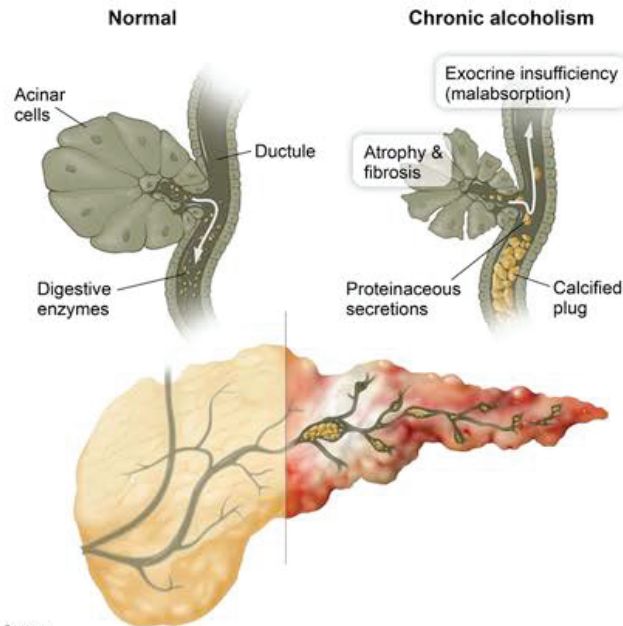
- ☐ A. ~~Bile salt malabsorption (11%)~~
- ☒ B. Digestive enzyme deficiency (70%)
- ☐ C. ~~Elevated portal venous pressure (1%)~~
- ☐ D. Excessive gastrin production (8%)
- ☐ E. ~~Immune-mediated enteropathy (2%)~~
- ☐ F. ~~Nutrient absorption interference by alcohol (4%)~~

Correct

 70%  
Answered correctly 47 secs  
Time Spent 01/30/2021  
Last Updated

### Exhibit Display

#### Pathogenesis of chronic alcoholic pancreatitis



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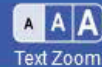
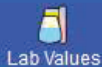
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Reset

New | Existing

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This patient's epigastric calcifications and history of alcohol use make **chronic alcoholic pancreatitis** the most likely diagnosis. It is thought that alcohol-related chronic pancreatitis develops in part due to alcohol-induced secretion of protein-rich fluid. These proteinaceous secretions can precipitate within the pancreatic ducts, forming **ductal plugs** that may **calcify** and be detectable on **abdominal imaging**.

Ductal obstruction by such concretions may cause **exocrine insufficiency** due to atrophy of the pancreatic acinar cells and pancreatic fibrosis. Pancreatic exocrine insufficiency (eg, failure to secrete adequate amylases, proteases, and lipases) leads to **malabsorption** with consequent **diarrhea/steatorrhea**.

**Weight loss** and bulky, frothy stools are typical clinical findings. This patient's abdominal pain is most likely due to the pancreatitis itself.

**(Choice A)** Bile salt malabsorption typically occurs with conditions affecting the terminal ileum (eg, ileal resection, Crohn ileitis). Patients may have diarrhea as a result of excessive bile salt accumulation in the colon (cholerheic enteropathy).

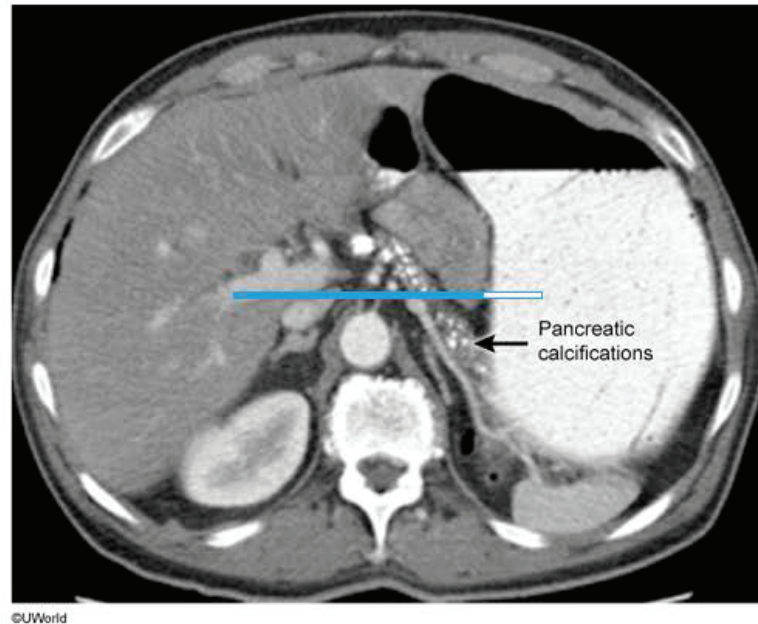
**(Choice C)** Portal hypertension (eg, due to liver cirrhosis) causes varices at sites of portocaval anastomoses, leading to anorectal varices, caput medusae over the abdomen, and esophageal varices. Bleeding esophageal varices can cause hematemesis and melena. Ascites is another sign of portal





Exhibit Display

Chronic pancreatitis



Zoom In Zoom Out Reset New | Existing My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

bleeding esophageal varices can cause hematemesis and melena. Ascites is another sign of portal hypertension.

**(Choice D)** Gastrinomas (duodenal/pancreatic gastrin-secreting neuroendocrine tumors) cause hydrochloric acid hypersecretion, which can result in multiple and/or refractory peptic ulcers. Patients may also have diarrhea/malabsorption as digestive enzymes become deactivated by high gastric acid output.

**(Choice E)** Celiac disease classically presents with malabsorption due to immune-mediated enteropathy involving the proximal small intestine. This condition is triggered by the ingestion of foods containing gluten (eg, wheat).

**(Choice F)** Chronic alcohol use may result in the interference of nutrient/vitamin absorption due to intestinal mucosal injury. However, this patient's abdominal pain and epigastric calcifications suggest that his diarrhea is most likely a consequence of chronic pancreatitis.

### Educational objective:

Diarrhea, weight loss, and epigastric calcifications in a patient with chronic alcoholism suggest chronic pancreatitis with resulting pancreatic exocrine insufficiency and malabsorption.

### References

- [Evaluation of chronic diarrhea.](#)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



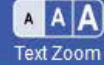
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Calculator



Reverse Color



Text Zoom



Settings

Laparotomy performed on a 35-year-old Caucasian male with abdominal pain shows chalky white lesions in the mesentery. Histologic evaluation of the lesions reveals fat cell destruction and calcium deposition. This patient most likely suffers from:

- ☐ A. Mesenteric ischemia
- ☐ B. Intestinal perforation
- ☐ C. Bacterial peritonitis
- ☐ D. Crohn's disease
- ☐ E. Acute pancreatitis
- ☐ F. Celiac disease

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



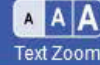
Notes



Calculator



Reverse Color



Text Zoom



Settings

Laparotomy performed on a 35-year-old Caucasian male with abdominal pain shows chalky white lesions in the mesentery. Histologic evaluation of the lesions reveals fat cell destruction and calcium deposition. This patient most likely suffers from:

- ☐ A. Mesenteric ischemia (10%)
- ☐ B. ~~Intestinal perforation~~ (1%)
- ☐ C. ~~Bacterial peritonitis~~ (2%)
- ☐ D. Crohn's disease (6%)
- ☒ E. Acute pancreatitis (75%)
- ☐ F. Celiac disease (2%)

Correct

 75%  
Answered correctly 01 min, 03 secs  
Time Spent 01/30/2021  
Last Updated

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

In acute pancreatitis, duct obstruction leads to stasis of pancreatic secretions and digestion of adipose cells by lipase. This results in formation of fatty acids that bind calcium ions and precipitate as insoluble calcium salts. The areas of focal necrosis and calcium precipitation induce an inflammatory reaction. If the pathologic process stops at this stage, benign **acute interstitial pancreatitis** develops. In this subtype of acute pancreatitis, the pancreas looks edematous on macroscopic examination. On light microscopy, interstitial edema, focal fat necrosis and calcium deposits are seen. If the inflammatory process continues, blood flow to the pancreatic acini is compromised as a result of the edema. Ischemia damages the acinar cells and causes abnormal intracellular activation of trypsin. Trypsin then activates other proteolytic enzymes, thus initiating autodigestion (autolysis) of pancreatic tissue. **Acute necrotic pancreatitis** develops. Destruction of blood vessel walls can cause hemorrhage into the necrotic areas.

Macroscopically, areas of white chalky fat necrosis are visible in the pancreatic tissue. They can spread onto the mesentery, omentum and other parts of abdominal cavity. Black areas of hemorrhage are also seen on gross examination.

**(Choice A)** In mesenteric ischemia an affected segment of the bowel is dusky red and congested. Subserosal ecchymoses, edema and/or well-defined areas of necrosis may be present.

**(Choice B)** Intestinal perforation (due to ulcer, mesenteric ischemia, tumor or inflammatory bowel disease)



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** In mesenteric ischemia an affected segment of the bowel is dusky red and congested.

Subserosal ecchymoses, edema and/or well-defined areas of necrosis may be present.

**(Choice B)** Intestinal perforation (due to ulcer, mesenteric ischemia, tumor or inflammatory bowel disease) is characterized by the presence of a defect in the intestinal wall along with signs of peritonitis.

**(Choice C)** Bacterial peritonitis is characterized by a dull-appearing peritoneal surface with areas of viscous white-yellow suppurative exudate.

**(Choice D)** In Crohn's disease, mesenteric fat extends along the serosa of an affected segment ("creeping fat"). The intestinal serosa looks dull-gray, edematous and granular. The mesentery of an involved segment may be edematous or fibrotic.

**(Choice F)** The serosa and mesentery of an involved bowel segment appear normal in celiac disease.

### Educational Objective:

In acute interstitial pancreatitis the pancreas is grossly edematous. Focal areas of fat necrosis, calcium deposition and interstitial edema are seen on light microscopy. In necrotizing (hemorrhagic) pancreatitis, chalky-white areas of fat necrosis interspersed with hemorrhage are seen on macroscopic examination.

Pathology

Gastrointestinal &amp; Nutrition

Acute pancreatitis

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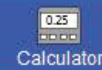
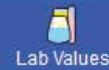
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In an animal experiment, mice proerythroblasts are cultured in 2 different growth media; the first medium is folate deficient, whereas the second (control) is supplemented with folic acid. Both media contain high concentrations of erythropoietin. Over 48 hours, cells in the control media proliferate and differentiate into reticulocytes, whereas in the folate-deficient media, cell proliferation is minimal, with the majority of cells undergoing apoptosis. In another experiment, a substance is added to the folate-deficient media, which prevents apoptosis and permits proliferation of the proerythroblasts. Which of the following is the most likely substance added to the growth medium?

- ☐ A. Cobalamin
- ☐ B. Cytosine
- ☐ C. Glutamine
- ☐ D. Homocysteine
- ☐ E. Thymidine

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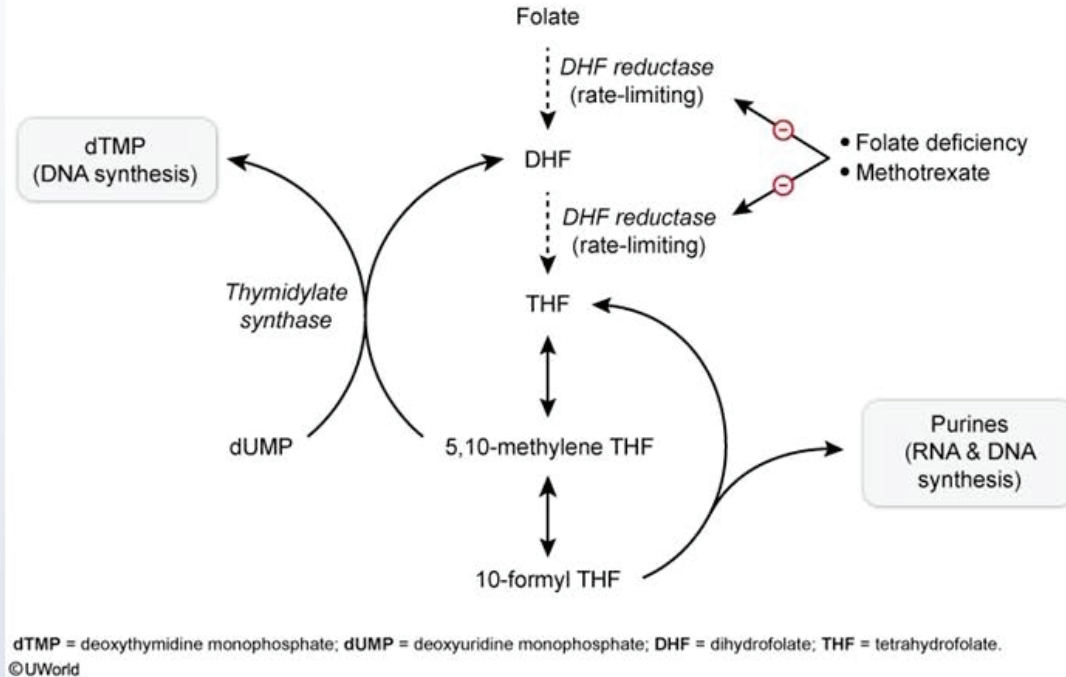
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- ☐ A. Cobalamin (33%)
- ☐ B. Cytosine (3%)
- ☐ C. Glutamine (3%)
- ☐ D. Homocysteine (17%)
- ☒ E. Thymidine (41%)

### Folate & nucleotide synthesis



Folate derivatives are crucial in the synthesis of nucleic acids (particularly thymine, but also purine bases).





Folate derivatives are crucial in the synthesis of nucleic acids (particularly thymine, but also purine bases), conversion of homocystine to methionine, and generation of one-carbon carriers (eg, S-adenosylmethionine) for methylation reactions. All biochemical functions of folate require the reduced **tetrahydrofolate** form of the vitamin, which is synthesized by dihydrofolate reductase (a rate-limiting step in folate metabolism).

The enzyme **thymidylate synthase** is responsible for converting deoxyuridine monophosphate (dUMP) to deoxythymidine monophosphate (**dTMP**). Although most enzymes involved in one-carbon metabolism maintain folate in its active tetrahydrofolate form, thymidylate synthase is unique in that it oxidizes 5,10-methylenetetrahydrofolate to **dihydrofolate**. This makes de novo thymidine synthesis particularly susceptible to folate-deficient conditions, as tetrahydrofolate must be continuously regenerated by dihydrofolate reductase.

In this experiment, inhibition of thymidylate synthase due to low folate conditions increases the ratio of dUMP to dTMP, causing the incorporation of uracil into DNA in place of thymidine. This leads to excessive activation of DNA repair mechanisms, resulting in double-stranded DNA breaks and apoptosis. Thymidine supplementation increases the amount of available thymidine and is capable of inhibiting apoptosis in folate-deficient cells.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice A)** Cobalamin is a necessary cofactor for methionine synthase, the enzyme that transfers a methyl group from 5-methyltetrahydrofolate to homocysteine, forming methionine and regenerating tetrahydrofolate. Cobalamin deficiency can cause folate to become trapped in 5-methyltetrahydrofolate form, resulting in secondary folate deficiency. However, cobalamin supplementation would not be of significant benefit in this patient as the primary folate deficiency prevents synthesis of tetrahydrofolate in the first place.

**(Choice B)** Cytosine is a pyrimidine base. Unlike thymine, it is not dependent on folate and can be synthesized in sufficient quantities under folate-deficient conditions.

**(Choice C)** Glutamine is a major source of nitrogen in the synthesis of purine and pyrimidine bases. However, glutamine supplementation would not ameliorate the cellular apoptosis induced by folate deficiency.

**(Choice D)** Homocysteine is an amino acid associated with endothelial cell injury and vascular inflammation. Levels are elevated in folate deficiency due to impaired conversion into methionine.

### Educational objective:

Folate deficiency inhibits the synthesis of nucleic acids, particularly the formation of deoxythymidine monophosphate (dTMP). This leads to defective DNA synthesis that characteristically causes increased



1



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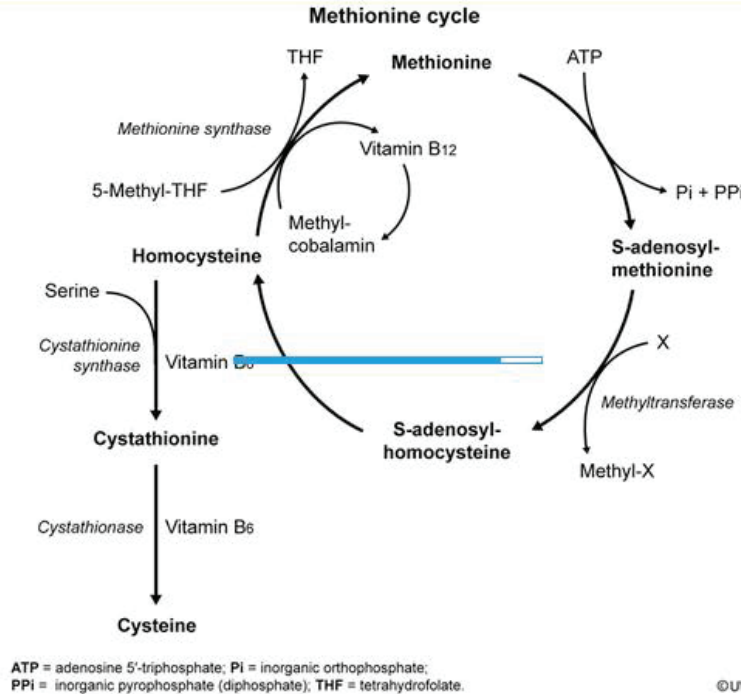


Suspend



End Block

Exhibit Display



Zoom In Zoom Out Reset New Existing My Notebook





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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### Educational objective:

Folate deficiency inhibits the synthesis of nucleic acids, particularly the formation of deoxythymidine monophosphate (dTMP). This leads to defective DNA synthesis that characteristically causes increased apoptosis of hemopoietic cells and megaloblastic anemia. Thymidine supplementation bypasses this enzyme and can reduce erythroid cell apoptosis.

### References



1



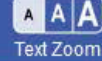
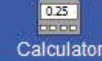
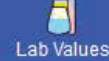
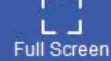
Feedback



Suspend



End Block



A 62-year-old man comes to the office due to worsening dysphagia. Three months ago, the patient started having difficulty swallowing large bites of solid food, and now he can swallow only liquids and mashed food. He has lost 9.1 kg (20 lb) since the onset of his symptoms. Medical history is significant for type 2 diabetes mellitus, hypercholesterolemia, and hypertension. The patient recently reduced the doses of his diabetic medications due to weight loss and lower blood glucose levels. He has no recent travel outside of the United States. Vital signs are normal. BMI is 29 kg/m<sup>2</sup>. Physical examination is normal. A barium swallow study reveals an esophageal mass that significantly narrows the lumen. Endoscopic biopsy reveals moderately differentiated tumor cells with keratin nests and pearls. This patient's condition is most likely related to which of the following risk factors?

- ☐ A. Alcohol consumption and tobacco smoking
- ☐ B. Cold beverage consumption
- ☐ C. Gastroesophageal reflux disease and esophagitis
- ☐ D. *Helicobacter pylori* infection
- ☐ E. Obesity and metabolic syndrome





Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

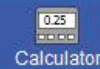
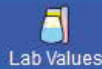
having difficulty swallowing large bites of solid food, and now he can swallow only liquids and mashed food. He has lost 9.1 kg (20 lb) since the onset of his symptoms. Medical history is significant for type 2 diabetes mellitus, hypercholesterolemia, and hypertension. The patient recently reduced the doses of his diabetic medications due to weight loss and lower blood glucose levels. He has no recent travel outside of the United States. Vital signs are normal. BMI is 29 kg/m<sup>2</sup>. Physical examination is normal. A barium swallow study reveals an esophageal mass that significantly narrows the lumen. Endoscopic biopsy reveals moderately differentiated tumor cells with keratin nests and pearls. This patient's condition is most likely related to which of the following risk factors?

- ☒ A. Alcohol consumption and tobacco smoking (86%)
- ☐ B. Cold beverage consumption (0%)
- ☐ C. Gastroesophageal reflux disease and esophagitis (9%)
- ☐ D. *Helicobacter pylori* infection (0%)
- ☐ E. Obesity and metabolic syndrome (3%)



End Block





### Risk factors for esophageal cancer

Squamous cell carcinoma	Adenocarcinoma
<ul style="list-style-type: none"><li>• Alcohol use</li><li>• Tobacco smoking</li><li>• N-nitroso-containing foods</li><li>• Underlying esophageal disease (achalasia, prior injury)</li></ul>	<ul style="list-style-type: none"><li>• Barrett esophagus</li><li>• Gastroesophageal reflux disease</li><li>• Obesity</li><li>• Tobacco use</li></ul>

This patient has **squamous cell carcinoma** (SCC), which is characterized by flattened polyhedral or ovoid epithelial cells with eosinophilic cytoplasm, keratin nests or **pearls** within or between cells, and intercellular bridging. **Esophageal SCC** typically presents with progressive solid-food dysphagia and weight loss. Chronic gastrointestinal blood loss may result in iron deficiency anemia.

The incidence of esophageal SCC is decreasing in the United States, with the highest incidence occurring in middle-aged and older individuals (age >50). The most significant risk factors for SCC in the United States include **cigarette smoking** and **alcohol intake**. In Asia, the chewing of betel nuts and consumption of foods containing N-nitroso compounds (often found in preserved or pickled vegetables) are commonly





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



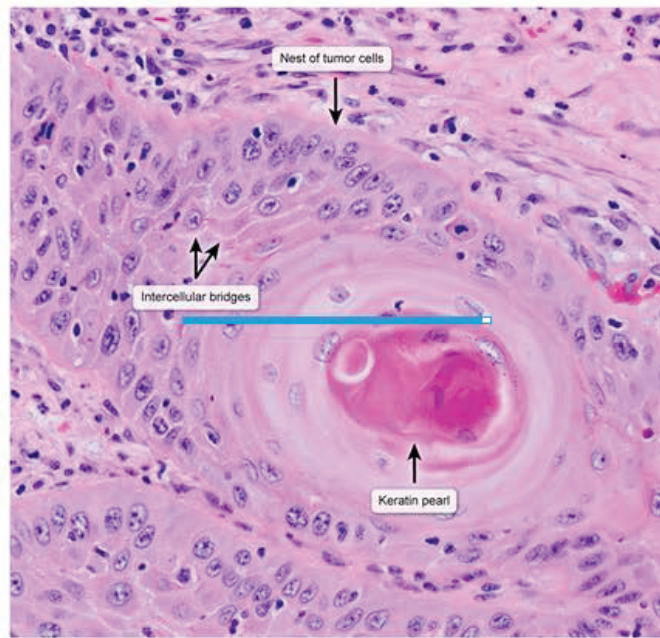
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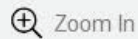
Settings

## Exhibit Display

## Squamous cell carcinoma



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Zoom Out



Reset



New



Existing



My Notebook

My Notebook



1



Feedback



Suspend



End Block



Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

in middle-aged and older individuals (age >50). The most significant risk factors for SCC in the United

States include **cigarette smoking** and **alcohol intake**. In Asia, the chewing of betel nuts and consumption of foods containing N-nitroso compounds (often found in preserved or pickled vegetables) are commonly associated with SCC. Other risk factors include preexisting esophageal disease (eg, achalasia, caustic injury) and ingestion of high-temperature liquids (**Choice B**).

(**Choice C**) Chronic gastroesophageal reflux disease and esophagitis can lead to **Barrett metaplasia** and can increase the risk for esophageal adenocarcinoma.

(**Choice D**) *Helicobacter pylori* infection, a common cause of gastritis, is associated with an increased risk of gastric adenocarcinoma. However, it is not associated with increased risk of the development of Barrett esophagus, esophageal adenocarcinoma, or esophageal SCC.

(**Choice E**) Obesity and metabolic syndrome are associated with increased risk of **esophageal adenocarcinoma**, likely because of increased acid reflux into the esophagus due to anatomic abnormalities.

### Educational objective:

Major risk factors for esophageal squamous cell carcinoma include smoking, excessive alcohol consumption, and intake of foods containing N-nitroso compounds.

Pathology      Gastrointestinal & Nutrition      Esophageal Cancer

Block Time Remaining: 00:20:49

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Feedback

Suspend

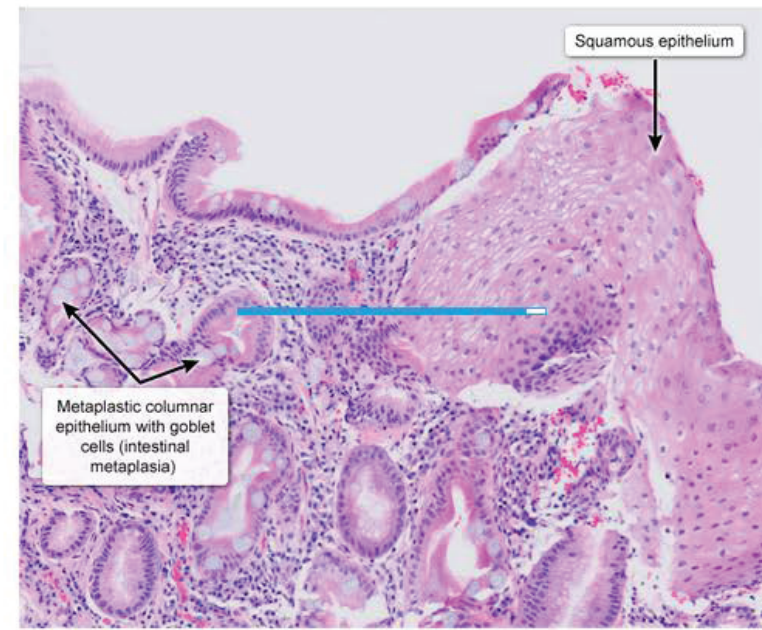
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In middle-aged and older individuals (age >50). The most significant risk factors for SCC in the United

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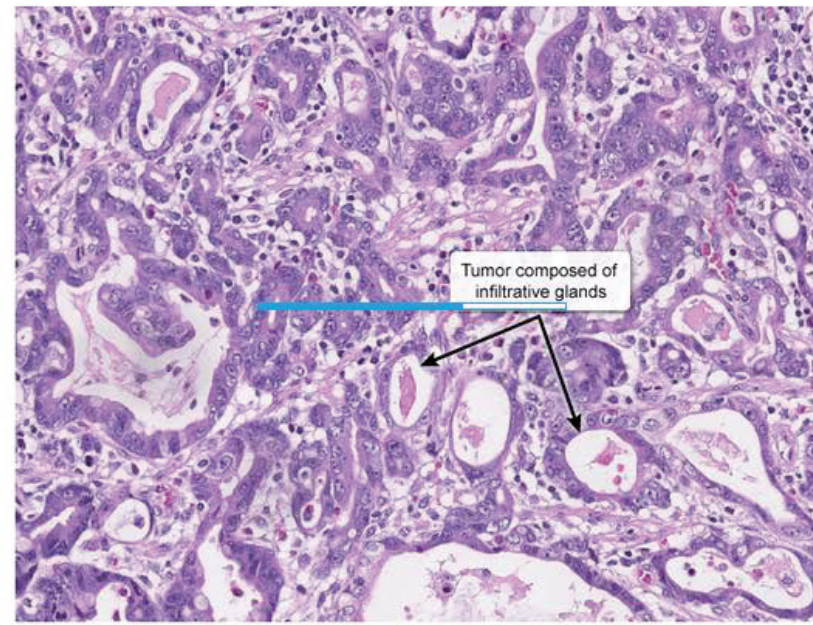
Barrett esophagus



In middle-aged and older individuals (age >50). The most significant risk factors for SCC in the United

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Esophageal adenocarcinoma



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 46-year-old man is brought to the emergency department by paramedics after an episode of large-volume hematemesis. He was going over some papers at work when he suddenly felt nauseated and started vomiting up bright red blood. Physical examination reveals a palpable spleen. Endoscopy shows bleeding esophageal varices. A liver biopsy performed 2 days later shows no abnormalities. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Acetaminophen toxicity
- ☐ B. Long-term alcohol consumption
- ☐ C. Budd-Chiari syndrome
- ☐ D. Constrictive pericarditis
- ☐ E. Portal vein thrombosis

**Submit**

0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom




Settings

A 46-year-old man is brought to the emergency department by paramedics after an episode of large-volume **hematemesis**. He was going over some papers at work when he suddenly felt nauseated and started vomiting up bright red blood. Physical examination reveals a **palpable spleen**. Endoscopy shows bleeding esophageal varices. A liver biopsy performed 2 days later shows **no abnormalities**. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Acetaminophen toxicity (3%)
- ☐ B. Long-term alcohol consumption (11%)
- ☐ C. Budd-Chiari syndrome (22%)
- ☐ D. Constrictive pericarditis (1%)
- ☒ E. Portal vein thrombosis (60%)

Correct

 60%  
Answered correctly 35 secs  
Time Spent 10/05/2020  
Last Updated

Feedback



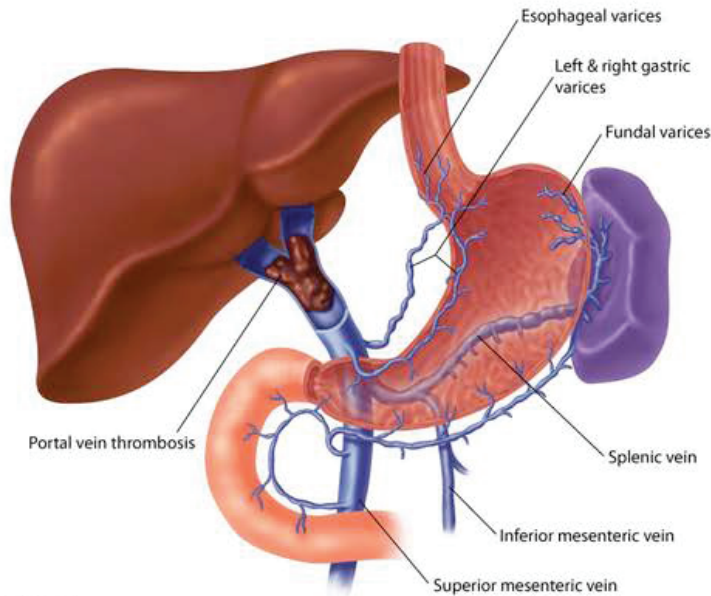
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### Exhibit Display

#### Portal vein thrombosis



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Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient is exhibiting signs of **portal hypertension**, including esophageal **varices** and **splenic enlargement**. Varices form in portal hypertension due to increased hydrostatic pressure in the portal system that causes blood to be shunted through portocaval anastomoses. This patient's **normal liver biopsy** indicates that a **presinusoidal process** is responsible for the portal hypertension. **Portal vein thrombosis** causes obstruction in portal venous flow upstream to the liver, causing portal hypertension while not affecting the liver parenchyma. **Ascites is uncommon** with portal vein thrombosis since sinusoidal hypertension does not develop.

**(Choice A)** Acetaminophen toxicity causes centrilobular hepatic necrosis and liver failure 24-48 hours following ingestion, depending on the amount consumed. This process would be obvious on liver biopsy.

**(Choice B)** Long-term alcohol consumption can cause hepatic cirrhosis, which can cause portal hypertension. However, hepatocyte injury and fibrosis would be evident on liver biopsy. Mallory-Weiss tears can also occur with heavy alcohol use, however, mucosal lacerations (not varices) would be seen on endoscopy.

**(Choice C)** In Budd-Chiari syndrome, there is occlusion of the hepatic vein, which drains blood from the liver and portal circulation into the systemic circulation. Liver biopsy shows centrilobular congestion and fibrosis.



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

endoscopy.

**(Choice C)** In Budd-Chiari syndrome, there is occlusion of the hepatic vein, which drains blood from the liver and portal circulation into the systemic circulation. Liver biopsy shows centrilobular congestion and fibrosis.

**(Choice D)** Constrictive pericarditis causes blood to back up in the systemic venous circulation due to decreased cardiac output. This increases pressure within the liver in much the same way as Budd-Chiari syndrome and would present with similar findings.

**Educational objective:**

Portal vein thrombosis causes portal hypertension, splenomegaly, and varicosities at portocaval anastomoses. It does not cause histologic changes to the hepatic parenchyma. Ascites is uncommon as the obstruction is presinusoidal; ascites typically only develops in conditions that cause sinusoidal hypertension.

Pathology

Gastrointestinal &amp; Nutrition

Esophageal varices

Subject

System

Topic

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Block Time Remaining: 00:21:24

TUTOR

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0



Feedback



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



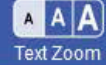
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 28-year-old man with vague abdominal pain, low-grade fever, and diarrhea is treated with antibiotics without significant improvement in his symptoms. Several weeks after symptom onset, the patient develops a skin lesion over the abdomen. His temperature is 37.8 C (100 F), blood pressure is 120/70 mm Hg, and pulse is 88/min. On physical examination, the abdomen is mildly distended and tender to palpation. Bowel contents appear to be draining to the surface of the skin in the right lower abdominal quadrant. This patient most likely suffers from which of the following conditions?

- ☐ A. Acute appendicitis
- ☐ B. Crohn disease
- ☐ C. Mesenteric adenitis
- ☐ D. Pseudomembranous colitis
- ☐ E. Ulcerative colitis

**Submit**

1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 28-year-old man with vague abdominal pain, low-grade fever, and diarrhea is treated with antibiotics without significant improvement in his symptoms. Several weeks after symptom onset, the patient develops a skin lesion over the abdomen. His temperature is 37.8 C (100 F), blood pressure is 120/70 mm Hg, and pulse is 88/min. On physical examination, the abdomen is mildly distended and tender to palpation. Bowel contents appear to be draining to the surface of the skin in the right lower abdominal quadrant. This patient most likely suffers from which of the following conditions?

- ☐ A. Acute appendicitis (7%)
- ☒ B. Crohn disease (68%)
- ☐ C. Mesenteric adenitis (11%)
- ☐ D. Pseudomembranous colitis (7%)
- ☐ E. Ulcerative colitis (5%)

Correct

68%  
Answered correctly15 secs  
Time Spent12/05/2020  
Last Updated

Block Time Remaining: 00:21:39

TUTOR

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

	Crohn disease	Ulcerative colitis
<b>Involvement</b>	<ul style="list-style-type: none"> <li>Anywhere mouth to anus (mostly ileum &amp; colon)</li> <li>Perianal disease with rectal sparing</li> <li>Skip lesions</li> </ul>	<ul style="list-style-type: none"> <li>Rectum (always) &amp; colon</li> <li>Continuous lesions</li> </ul>
<b>Microscopy</b>	<ul style="list-style-type: none"> <li>Noncaseating granulomas</li> </ul>	<ul style="list-style-type: none"> <li>No granulomas</li> </ul>
<b>Gross findings</b>	<ul style="list-style-type: none"> <li>Transmural inflammation</li> <li>Linear mucosal ulcerations</li> <li>Cobblestoning, creeping fat</li> </ul>	<ul style="list-style-type: none"> <li>Mucosal &amp; submucosal inflammation</li> <li>Pseudopolyps</li> </ul>
<b>Clinical manifestations</b>	<ul style="list-style-type: none"> <li>Abdominal pain (often RLQ)</li> <li>Watery diarrhea (bloody if colitis)</li> </ul>	<ul style="list-style-type: none"> <li>Abdominal pain (varying locations)</li> <li>Bloody diarrhea</li> </ul>
<b>Intestinal complications</b>	<ul style="list-style-type: none"> <li>Fistulae, abscesses</li> <li>Strictures (bowel obstruction)</li> </ul>	<ul style="list-style-type: none"> <li>Toxic megacolon</li> </ul>

RLQ = right lower quadrant.



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**RLQ** = right lower quadrant.

Crohn disease and ulcerative colitis are collectively referred to as inflammatory bowel disease. They may have similar clinical manifestations, but they also have key distinguishing features (Table).

**Crohn disease** typically presents with **prolonged diarrhea** and **abdominal pain**. Diarrhea can be bloody if the colon is involved. Constitutional symptoms (eg, low-grade fever, fatigue), malabsorption, and weight loss are also common. **Transmural inflammation** of the bowel wall may result in the formation of fistulas and fibrotic strictures, causing bowel obstruction. Fistulas can form between 2 adjacent loops of bowel (enteroenteric fistula), between the bowel and another organ (eg, bladder, vagina), or between the bowel and skin of the abdominal wall (**enterocutaneous fistula**). Perianal fistulas and abscesses are also often seen.

Ulcerative colitis typically presents with bloody diarrhea associated with abdominal pain and tenesmus. Fistula formation does not usually occur as inflammation is confined to the mucosa and submucosa  
**(Choice E).**

**(Choice A)** Right lower quadrant abdominal pain, fever, nausea, and vomiting are classic symptoms of acute appendicitis. If untreated, appendicitis may progress to peritonitis or abscess formation, but fistula formation is not common.



1



Feedback



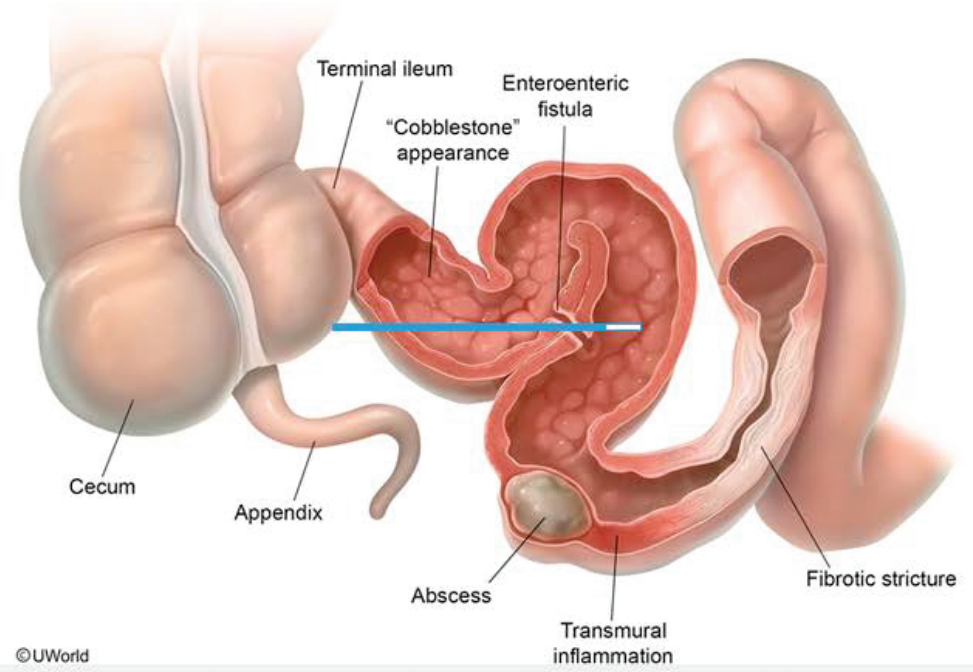
Suspend



End Block

### Exhibit Display

## Crohn disease



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Zoom Out

Reset

New | Existing

My Notebook





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** Right lower quadrant abdominal pain, fever, nausea, and vomiting are classic symptoms of acute appendicitis. If untreated, appendicitis may progress to peritonitis or abscess formation, but fistula formation is not common.

**(Choice C)** Mesenteric adenitis most often occurs in children age 5-14. Many cases are thought to be associated with *Yersinia enterocolitica* infection. Clinical manifestations may include fever, right lower quadrant abdominal pain, and nausea/vomiting, but fistulas are not characteristic.

**(Choice D)** Pseudomembranous colitis is typically caused by *Clostridium difficile* infection and presents with diarrhea, abdominal pain, and fever in a patient who has recently been hospitalized or treated with antibiotics. Fistulas are not typically seen.

### Educational objective:

Crohn disease typically presents with prolonged diarrhea and abdominal pain. Constitutional symptoms (eg, low-grade fever, fatigue), malabsorption, and weight loss are also common. Transmural inflammation of the bowel wall may result in the formation of fistulas (eg, enteroenteric, enterocutaneous), abscesses, and fibrotic strictures.

### References

- [Diagnosis and management of Crohn's disease.](#)



1



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 46-year-old Caucasian male who presented with abdominal pain is diagnosed with a rare vascular tumor. This type of tumor is oftentimes associated with past arsenic or polyvinyl chloride exposure. Immunohistochemical staining of the tumor cells is positive for the CD 31 cell marker. The patient most likely has which of the following conditions?

- ☐ A. Cavernous hemangioma
- ☐ B. Pyogenic granuloma
- ☐ C. Cystic hygroma
- ☐ D. Port-wine stain
- ☐ E. Kaposi's sarcoma
- ☐ F. Lymphangiosarcoma
- ☐ G. Liver angiosarcoma
- ☐ H. Vascular ectasia
- ☐ I. Glomus tumor





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

tumor. This type of tumor is oftentimes associated with past arsenic or polyvinyl chloride exposure.

Immunohistochemical staining of the tumor cells is positive for the CD 31 cell marker. The patient most likely has which of the following conditions?

- ☐ A. Cavernous hemangioma (4%)
- ☐ B. Pyogenic granuloma (1%)
- ☐ C. Cystic hygroma (1%)
- ☐ D. Port-wine stain (2%)
- ☐ E. Kaposi's sarcoma (2%)
- ☐ F. Lymphangiosarcoma (8%)
- ☒ G. Liver angiosarcoma (76%)
- ☐ H. Vascular ectasia (1%)
- ☐ I. Glomus tumor (2%)



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

## Explanation

This patient has a carcinogen-related neoplasm composed of cells that express CD 31, which is PECAM1 (platelet endothelial cell adhesion molecule). PECAM1, a member of the immunoglobulin family of proteins, is expressed on the surface of endothelial cells and functions in leukocyte migration through the endothelium. The patient's tumor thus appears to have arisen from vascular endothelial cells. The most likely diagnosis is liver angiosarcoma, a rare malignant vascular endothelial cell neoplasm that is associated with carcinogen exposure. Implicated chemicals include arsenic (exposure to pesticides), thorotrast (a former radioactive contrast medium), and polyvinyl chloride (a plastic widely used in industry).

**Educational Objective:**

Hepatic angiosarcoma is associated with exposure to carcinogens such as arsenic, thorotrast, and polyvinyl chloride. Tumor cells express CD 31, an endothelial cell marker.

Pathology

Gastrointestinal &amp; Nutrition

Hepatocellular cancer

Subject

System

Topic

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0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 68-year-old woman is evaluated after recurrent episodes of bright red blood per rectum. She has had no abdominal pain, nausea, vomiting, or hematemesis. Her medical conditions include hypertension and obesity. She is a smoker, has a sedentary lifestyle, and consumes processed food and red meat frequently. Abdominal examination shows no abnormalities. Colonoscopy reveals numerous mucosal outpouchings in the sigmoid colon, and sigmoid colectomy is performed. Histopathology of this patient's colonic lesions is most likely to reveal which of the following findings?

- ☐ A. Absence of muscularis propria
- ☐ B. Ectopic gastric mucosa
- ☐ C. Neoplastic mucosal growth
- ☐ D. Neural plexus lacking ganglion cells
- ☐ E. Normal colonic layers

**Submit**

1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 68-year-old woman is evaluated after recurrent episodes of bright red blood **per rectum**. She has had no abdominal pain, nausea, vomiting, or hematemesis. Her medical conditions include hypertension and **obesity**. She is a smoker, has a sedentary lifestyle, and consumes processed food and red meat frequently. Abdominal examination shows no abnormalities. Colonoscopy reveals numerous mucosal **outpouchings** in the sigmoid colon, and sigmoid colectomy is performed. Histopathology of this patient's colonic lesions is most likely to reveal which of the following findings?

- ☒ A. Absence of muscularis propria (47%)
- ☐ B. Ectopic gastric mucosa (3%)
- ☐ C. Neoplastic mucosal growth (25%)
- ☐ D. Neural plexus lacking ganglion cells (1%)
- ☐ E. Normal colonic layers (21%)

Correct

 47%  
Answered correctly 38 secs  
Time Spent 02/19/2021  
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Block Time Remaining: 00:22:50

TUTOR

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Feedback



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End Block

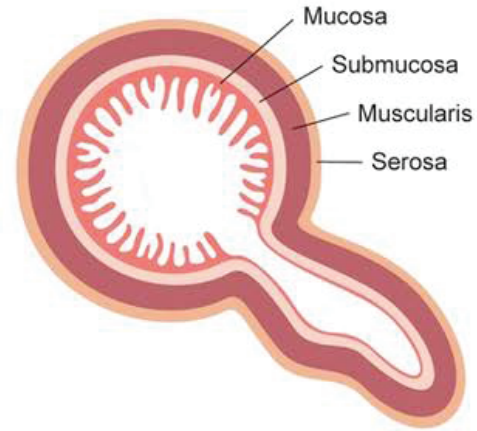


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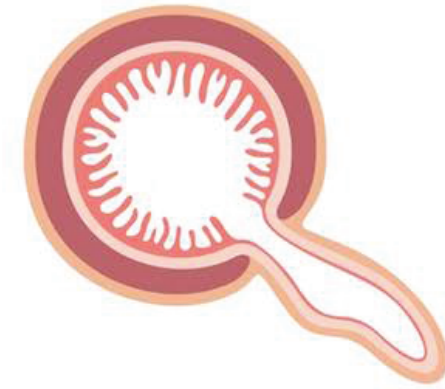
True & false diverticula

True diverticulum

Pseudodiverticulum



Examples:  
Meckel diverticula,  
normal appendix



Examples:  
Zenker esophageal diverticula,  
diverticulosis

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Reset

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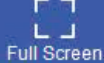
My Notebook



Mark

Previous

Next



Full Screen



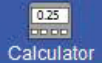
Tutorial



Lab Values



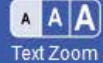
Notes



Calculator



Reverse Color



Text Zoom



Settings

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This elderly patient with hematochezia and abnormal outpouchings from the colonic lumen has **diverticulosis**. **Diverticulosis** most commonly affects the sigmoid colon and is usually seen in individuals age >60. Most patients are asymptomatic, but some may present with **painless hematochezia** due to disruption of the arterioles (vasa recta) adjacent to the diverticula. Diverticula can also become inflamed (ie, diverticulitis), causing left lower quadrant abdominal pain, low-grade fever, and constipation or diarrhea.

Diverticula of the gastrointestinal tract may be classified according to morphology; true diverticula include all 3 layers of the gut wall and are often formed during embryologic development. **False diverticula** occur when the **mucosa and submucosa herniate** through areas of **focal weakness in the muscularis**.

Exaggerated contractions of colonic smooth muscle segments are responsible for colonic diverticulosis; the resultant increased intraluminal pressure causes herniation and false diverticula formation. Most diverticula acquired during adult life are false (eg, Zenker diverticulum of the upper esophagus).

**(Choices B and E)** Congenital colonic diverticulosis and Meckel diverticula are formed during embryologic development and are true diverticula containing all three layers of the gut wall. Congenital colonic diverticula are extremely rare and typically occur as a single, large diverticulum. Meckel diverticula often contain heterotopic gastric or pancreatic mucosa, and may cause bleeding, but are located in the small



Feedback



Suspend



End Block



Mark

Previous

Next



Full Screen



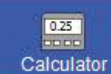
Tutorial



Lab Values



Notes



Calculator



Reverse Color



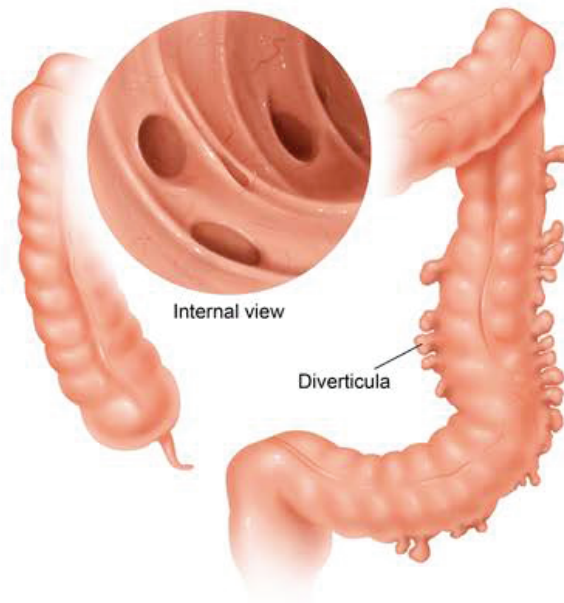
Text Zoom



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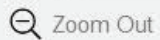
## Diverticulosis



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New



Existing



My Notebook

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1



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choices B and E)** Congenital colonic diverticulosis and Meckel diverticula are formed during embryologic development and are true diverticula containing all three layers of the gut wall. Congenital colonic diverticula are extremely rare and typically occur as a single, large diverticulum. Meckel diverticula often contain heterotopic gastric or pancreatic mucosa, and may cause bleeding, but are located in the small intestine; symptoms (ie, pain, nausea, vomiting) typically present in early childhood.

**(Choice C)** Neoplastic mucosal growth causes colonic polyps, which are solid protuberances into the colonic lumen (rather than the outpouching away from the lumen seen in diverticulosis).

**(Choice D)** Congenital aganglionic megacolon (Hirschsprung disease) results from the failure of neural crest cells to migrate to the colon, resulting in an aganglionic segment and severe constipation. This disease manifests in infancy with failure to pass meconium.

### Educational objective:

Colonic diverticula often involve the sigmoid colon and develop due to exaggerated contractions of colonic smooth muscle segments. This results in increased intraluminal pressure, causing outpouching of the mucosa and submucosa through the muscularis (false diverticula). Individuals (typically age >60) may be asymptomatic or have hematochezia or diverticulitis.



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 60-year-old woman comes to the office with persistent, profuse mucoid diarrhea. Despite not eating much for the past 2 days, her diarrhea has not decreased, but she has no other symptoms. The patient has not had age-appropriate colon cancer screening. Family history is unremarkable. She does not use tobacco, alcohol, or illicit drugs. Vital signs and cardiopulmonary examination are normal. The abdomen is soft and nondistended. There is no hepatosplenomegaly. Laboratory studies show hypokalemia and microcytic anemia. Colonoscopy reveals a 2.5-cm, cauliflower-like mass in the sigmoid colon. The mass is resected and the histopathology of the lesion is shown in the [exhibit](#). Which of the following is the most likely diagnosis in this patient?

- ☐ A. Carcinoid tumor
- ☐ B. Hamartomatous polyp
- ☐ C. Hyperplastic polyp
- ☐ D. Signet ring cell carcinoma
- ☐ E. Villous adenoma



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

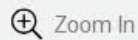
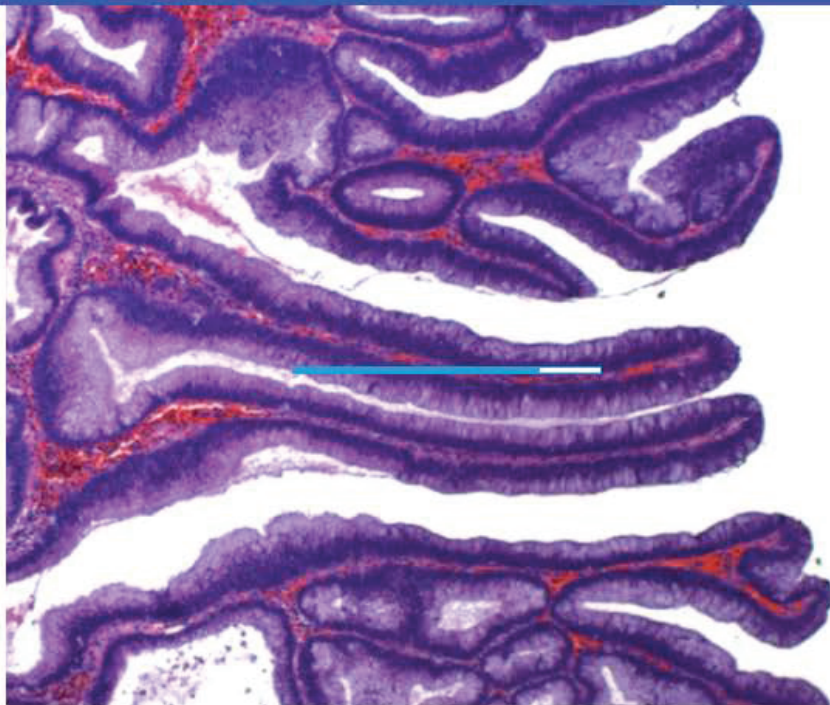


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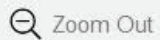


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Feedback



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End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

much for the past 2 days, her diarrhea has not decreased, but she has no other symptoms. The patient has not had age-appropriate colon cancer screening. Family history is unremarkable. She does not use tobacco, alcohol, or illicit drugs. Vital signs and cardiopulmonary examination are normal. The abdomen is soft and nondistended. There is no hepatosplenomegaly. Laboratory studies show **hypokalemia** and **microcytic anemia**. Colonoscopy reveals a 2.5-cm, cauliflower-like mass in the sigmoid colon. The mass is resected and the histopathology of the lesion is shown in the **exhibit**. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Carcinoid tumor (7%)
- ☐ B. Hamartomatous polyp (7%)
- ☐ C. Hyperplastic polyp (7%)
- ☐ D. Signet ring cell carcinoma (1%)
- ☒ E. Villous adenoma (75%)

Correct

75%



01 min, 33 secs



01/06/2021

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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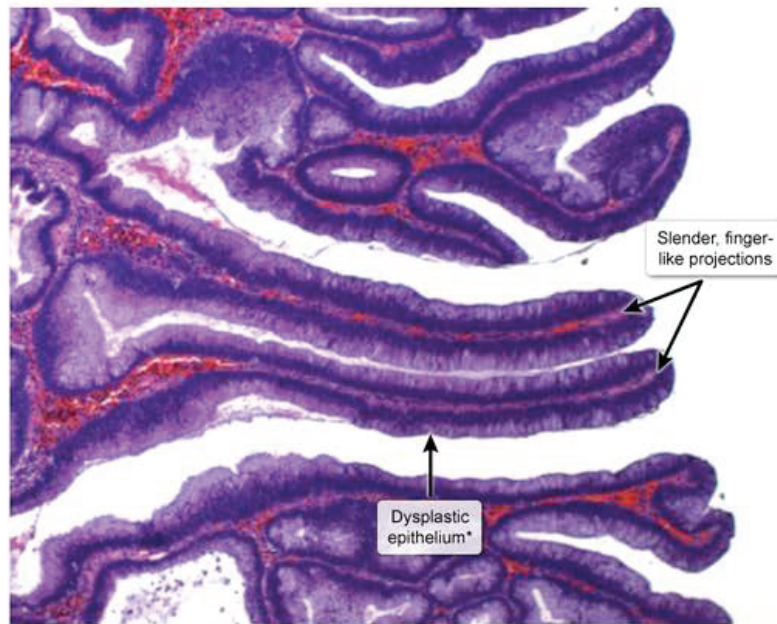
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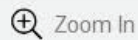
## Exhibit Display

## Villous adenoma

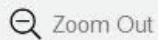


\*Crowded cells with dark, elongated nuclei

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\*Crowded cells with dark, elongated nuclei

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Biopsy of this patient's mass demonstrates long glands with finger-like (villous) projections extending from the surface as well as dysplastic epithelium, which are characteristic of a **villous adenoma**. A villous adenoma is often large and sessile and can have velvety or cauliflower-like projections. By contrast, a **tubular adenoma** is composed of dysplastic colonic mucosal cells that form tube-shaped glands and tends to be smaller and pedunculated. A mixture of these 2 types indicates a tubulovillous adenoma. Of these, villous adenomas are the most likely to undergo **malignant transformation**.

Adenomas in the colon can cause occult or visible bleeding, leading to iron-deficiency anemia. Large polyps may occasionally cause partial obstruction with pain, constipation, and abdominal distension. In addition, villous adenomas can produce large quantities of prostaglandin E2, which results in **increased mucin** production and a **secretory diarrhea** characterized by watery, mucinous stools. Mucin is a potassium-rich glycoprotein; excessive production can result in **hypoproteinemia** and **hypokalemia**.

**(Choice A)** Intestinal **carcinoids** can cause diarrhea and are often associated with additional symptoms such as flushing, wheezing, and vascular telangiectasia when they metastasize. Histopathology is typified by insular (nesting) masses of small, round cells with peripheral palisading, granular cytoplasm, small nucleoli, and salt-and-pepper chromatin.



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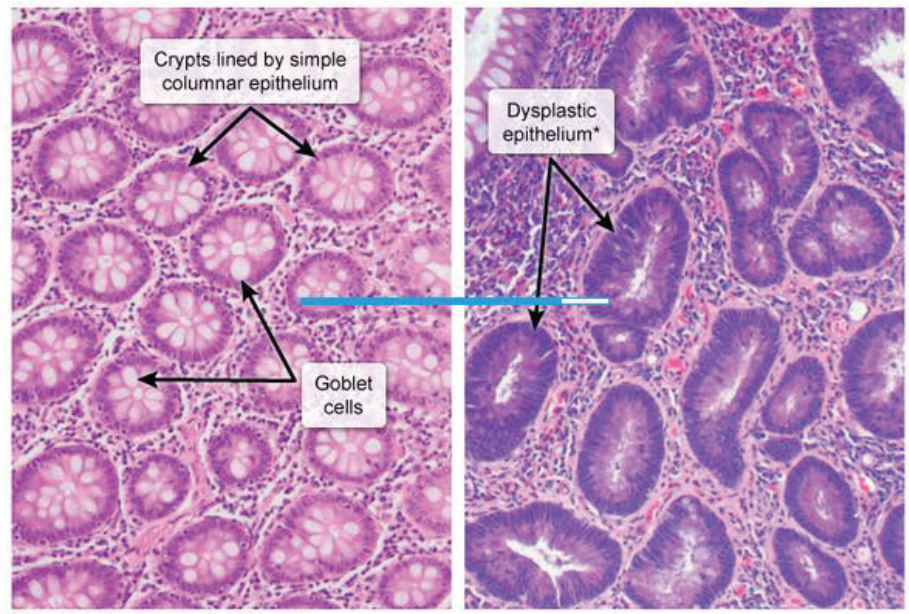
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Exhibit Display

Normal colonic mucosa

Tubular adenoma



\*Crowded cells with dark, elongated nuclei

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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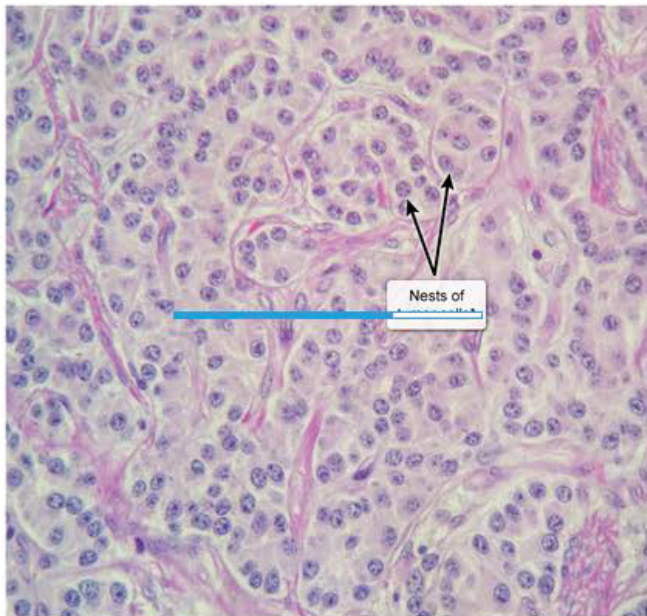
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## Exhibit Display

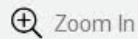
## Gastric well-differentiated neuroendocrine (carcinoid) tumor



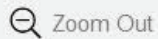
Nests of

\*Round nuclei, eosinophilic cytoplasm, and "salt and pepper" chromatin

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Previous



Next



Full Screen



Tutorial



Lab Values



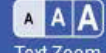
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Settings

nucleoli, and salt-and-pepper chromatin.

**(Choice B)** **Hamartomatous polyps** consist of disorganized mucosal glands, smooth muscle, and connective tissue. They may occur sporadically or in Peutz-Jeghers syndrome or juvenile polyposis. These polyps can cause bleeding and intussusception, but not secretory diarrhea.

**(Choice C)** **Hyperplastic polyps** are characterized by a proliferation of nondysplastic epithelial cells resulting in a serrated or "sawtoothed" architecture seen in the upper parts of the crypts. They are typically small lesions and almost always asymptomatic.

**(Choice D)** Signet ring cell carcinoma can occur in different locations, such as the **stomach**, breast, ovary, and colorectal area. Tumor cells contain abundant mucins that push the nuclei to the periphery and give the tumor cells their characteristic appearance.

### Educational objective:

Adenomatous polyps are either tubular, villous, or tubulovillous, depending on their histologic appearance. Villous adenomas tend to be larger, sessile, and more severely dysplastic than tubular adenomas. Villous adenomas can cause a secretory diarrhea from increased mucin production; patients may develop hypoproteinemia and hypokalemia.



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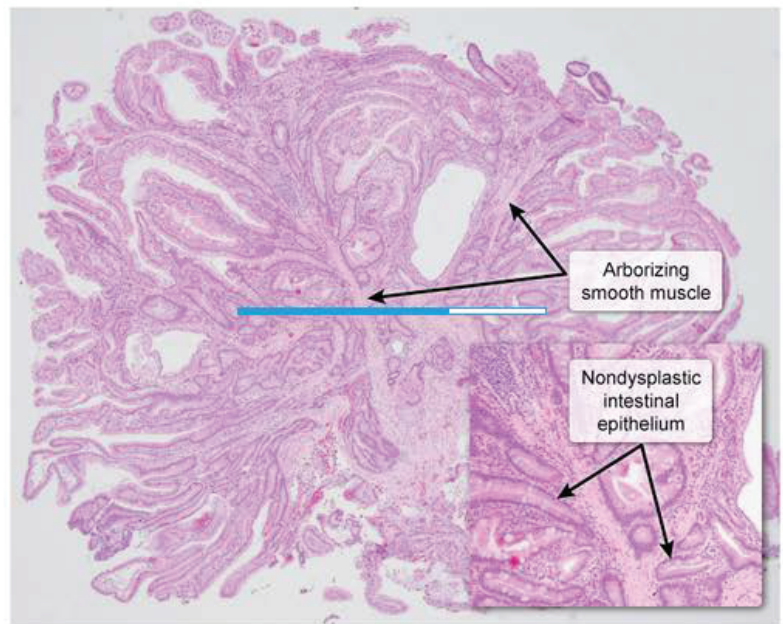
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nucleoli, and salt-and-pepper chromatin.

Exhibit Display

Hamartomatous polyp of Peutz-Jeghers syndrome



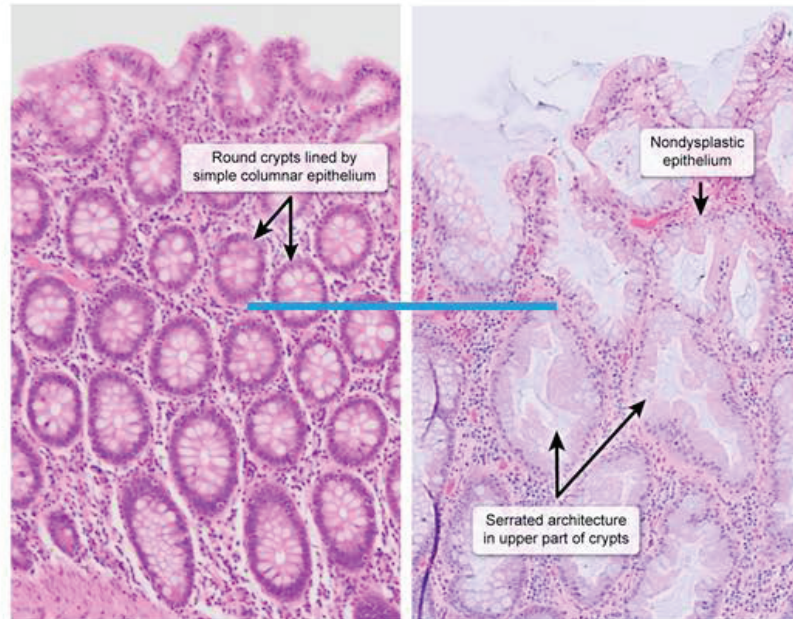
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nucleoli, and salt-and-pepper chromatin.

Exhibit Display

Normal colonic mucosa

Hyperplastic polyp

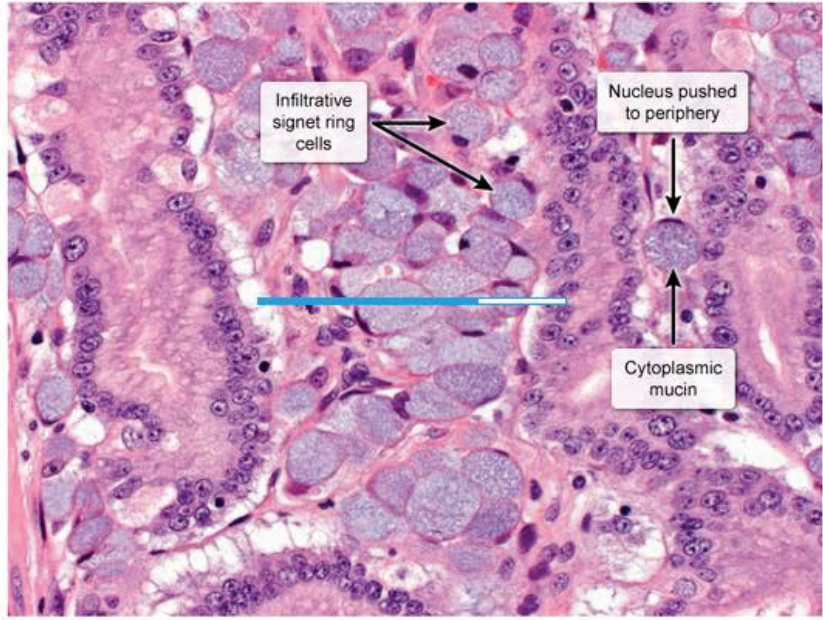


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nucleoli, and salt-and-pepper chromatin.

Exhibit Display

Diffuse-type gastric adenocarcinoma



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 46-year-old woman with a history of hiatal hernia and severe gastroesophageal reflux undergoes antireflux surgery. The reflux symptoms were refractory to medical therapy, so an endoscopic fundoplication procedure is performed. During surgery, the hiatal defect is repaired, and the gastric fundus is mobilized and wrapped around the lower esophagus to reinforce the lower esophageal sphincter. No esophageal or gastric injuries occurred, but a neural structure traversing the esophageal hiatus of the diaphragm was inadvertently injured. Which of the following is the most likely potential effect of this operative injury?

- ☐ A. Delayed gastric emptying
- ☐ B. Diaphragmatic paralysis
- ☐ C. Fecal incontinence
- ☐ D. Gastric acid hypersecretion
- ☐ E. Permanent loss of intestinal peristalsis

**Submit**

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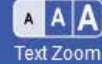
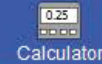
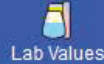
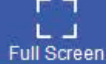
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A 46-year-old woman with a history of hiatal hernia and severe gastroesophageal reflux undergoes antireflux surgery. The reflux symptoms were refractory to medical therapy, so an endoscopic fundoplication procedure is performed. During surgery, the hiatal defect is repaired, and the gastric fundus is mobilized and wrapped around the lower esophagus to reinforce the lower esophageal sphincter. No esophageal or gastric injuries occurred, but a neural structure traversing the esophageal hiatus of the diaphragm was inadvertently injured. Which of the following is the most likely potential effect of this operative injury?

- ☒ A. Delayed gastric emptying (44%)
- ☐ B. Diaphragmatic paralysis (38%)
- ☐ C. Fecal incontinence (1%)
- ☐ D. Gastric acid hypersecretion (8%)
- ☐ E. Permanent loss of intestinal peristalsis (7%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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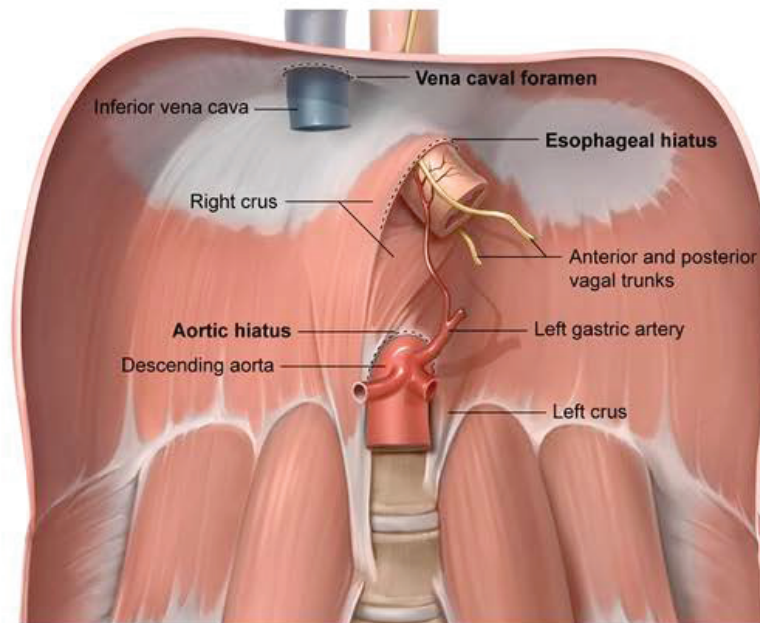
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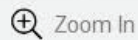
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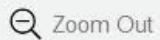
## Diaphragmatic apertures



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1



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**Fundoplication** is a surgical procedure used to treat refractory gastroesophageal reflux associated with an esophageal **hiatal hernia**. In the procedure, the esophageal hiatus is tightened, and the gastric fundus is wrapped around the lower esophageal sphincter, thereby preventing gastric acid from entering the esophagus.

However, the **anterior and posterior vagal trunks** (branches of the vagus nerve) also pass through the esophageal hiatus and are vulnerable to injury during fundoplication. These nerves supply parasympathetic innervation to the gastrointestinal tract and stimulate gastric muscle contraction and motility. Injury to the vagal trunks can lead to **delayed gastric emptying** (ie, gastroparesis), manifesting with abdominal pain, early satiety, and postprandial emesis.

**(Choice B)** The phrenic nerve innervates the diaphragm; it originates from the C3-C5 nerve roots and passes through the mediastinum between the heart and the lungs. It is unlikely to be injured during fundoplication because its terminal motor branches transit the venal caval foramen, not the esophageal hiatus.

**(Choice C)** Tonic contraction of the **pelvic floor muscles** (eg, levator ani) is necessary for preventing fecal incontinence. They receive parasympathetic innervation from the pelvic splanchnic nerves, not the vagus nerve, and their function would be unaffected by vagal injury.



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

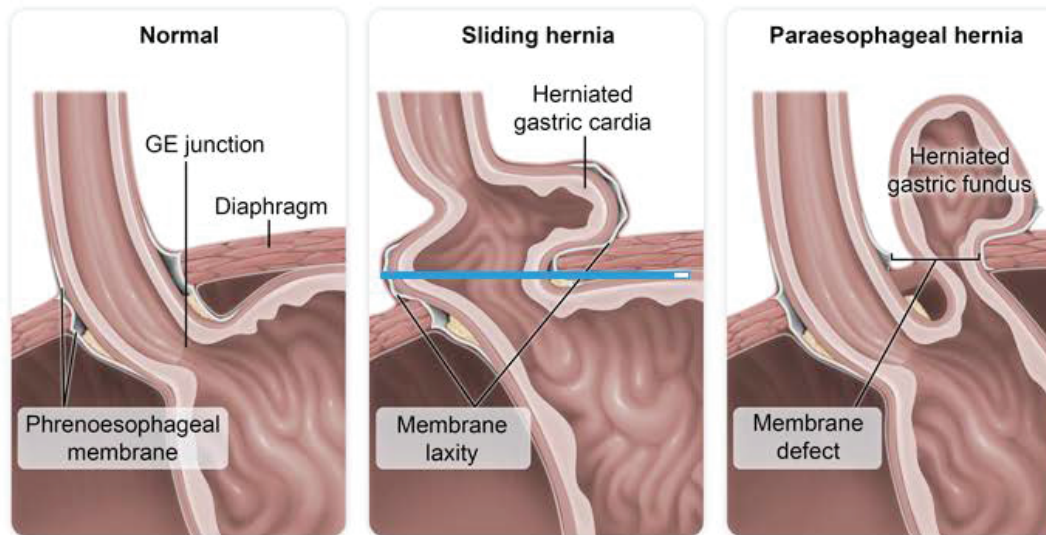
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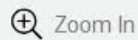
Fundoplication is a surgical procedure used to treat refractory gastroesophageal reflux associated with an

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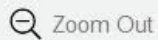
## Hiatal hernia



GE = gastroesophageal.  
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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

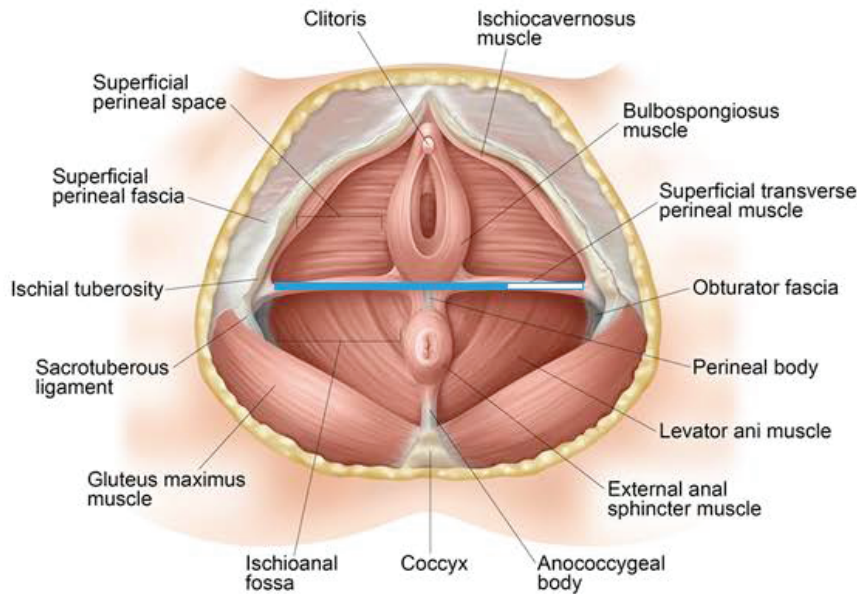
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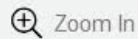
Fundoplication is a surgical procedure used to treat refractory gastroesophageal reflux associated with an

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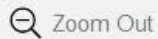
## Pelvic floor muscles



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1



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Mark



Previous



Next



Full Screen



Tutorial



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Notes



Calculator



Reverse Color



Text Zoom



Settings

hiatus.

**(Choice C)** Tonic contraction of the **pelvic floor muscles** (eg, levator ani) is necessary for preventing fecal incontinence. They receive parasympathetic innervation from the pelvic splanchnic nerves, not the vagus nerve, and their function would be unaffected by vagal injury.

**(Choice D)** The vagus nerve stimulates gastric parietal cell production of hydrochloric acid; injury may therefore lead to decreased gastric acid secretion (ie, hypochlorhydria), not increased secretion.

**(Choice E)** Intestinal peristalsis is mediated largely by the enteric nervous system. Although vagus nerve injury may cause transient intestinal dysmotility ~~due to sudden loss of parasympathetic input~~, it would not cause long-term dysfunction.

### Educational objective:

Branches of the vagus nerve (ie, anterior and posterior vagal trunks) pass through the esophageal hiatus. Damage to these branches, which can occur during esophageal hiatal hernia repair (eg, fundoplication), may result in delayed gastric emptying and gastric hypochlorhydria.

### References

- **Central nervous system control of gastrointestinal motility and secretion and modulation of gastrointestinal functions**



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



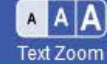
Notes



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Settings

A 40-year-old man comes to the office with pain on defecation. The pain is sharp and severe but subsides within minutes of passing the bowel movement. He often sees spots of bright red blood on the toilet paper. The patient has chronic constipation and has not taken laxatives or increased his fluid intake to compensate. He has no fever, night sweats, diarrhea, or unexpected weight loss. Past medical history is notable for chronic low back pain following a motor vehicle accident, for which he takes a scheduled dose of pain relievers. The patient has smoked a pack of cigarettes daily for the last 20 years but does not use alcohol or illicit drugs. He is married and has no outside sexual contacts. Vital signs are normal. The abdomen is soft and nontender with no hepatosplenomegaly. Rectal examination is likely to show a tear at which of the following locations?

- ☐ A. Anterior midline distal to the dentate line
- ☐ B. Anterior midline proximal to the dentate line
- ☐ C. Bilateral distal to the dentate line
- ☒ D. Lateral distal to the dentate line
- ☐ E. Lateral proximal to the dentate line



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

within minutes or passing the bowel movement. He often sees spots of bright red blood on the toilet paper.

The patient has chronic constipation and has not taken laxatives or increased his fluid intake to compensate. He has no fever, night sweats, diarrhea, or unexpected weight loss. Past medical history is notable for chronic low back pain following a motor vehicle accident, for which he takes a scheduled dose of pain relievers. The patient has smoked a pack of cigarettes daily for the last 20 years but does not use alcohol or illicit drugs. He is married and has no outside sexual contacts. Vital signs are normal. The abdomen is soft and nontender with no hepatosplenomegaly. Rectal examination is likely to show a tear at which of the following locations?

- ☐ A. Anterior midline distal to the dentate line
- ☐ B. Anterior midline proximal to the dentate line
- ☐ C. Bilateral distal to the dentate line
- ☐ D. Lateral distal to the dentate line
- ☐ E. Lateral proximal to the dentate line
- ☐ F. Posterior midline distal to the dentate line



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compensate. He has no fever, night sweats, diarrhea, or unexpected weight loss. Past medical history is notable for chronic low back pain following a motor vehicle accident, for which he takes a scheduled dose of pain relievers. The patient has smoked a pack of cigarettes daily for the last 20 years but does not use alcohol or illicit drugs. He is married and has no outside sexual contacts. Vital signs are normal. The abdomen is soft and nontender with no hepatosplenomegaly. Rectal examination is likely to show a tear at which of the following locations?

- ☐ A. Anterior midline distal to the dentate line (12%)
- ☐ B. Anterior midline proximal to the dentate line (6%)
- ☐ C. Bilateral distal to the dentate line (5%)
- ☐ D. Lateral distal to the dentate line (11%)
- ☐ E. Lateral proximal to the dentate line (3%)
- ☒ F. Posterior midline distal to the dentate line (59%)

Correct

59%



53 secs



10/29/2020

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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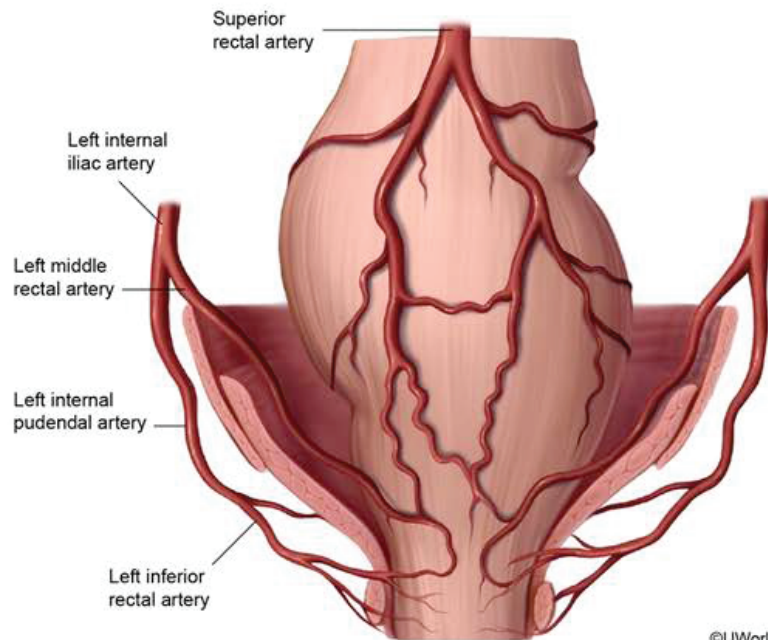
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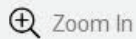
Settings

## Exhibit Display

## Anorectal arterial supply



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient has sharp pain and bright red rectal bleeding on defecation, suggesting an **anal fissure**. Anal fissures are due to stretching of the mucosa and are characterized by longitudinal tears in the anal canal distal to the dentate line (**Choice B**). Spasm of the sphincter can contribute to the pain and create tension across the wound, leading to a chronic fissure. Most fissures are related to chronic constipation with high anal pressures and passage of hard stools. They can also be seen with frequent diarrhea or anal sexual intercourse. In some cases, the pain may be so severe that patients withhold bowel movements, thereby exacerbating the constipation.

The majority of fissures, especially those causing prolonged symptoms, occur at the **posterior midline** of the anal verge. This is likely due to the relatively poor perfusion of the posterior anal canal, which makes its mucosa sensitive to trauma and slows healing times. Anterior midline fissures are less common, but may occur due to mechanical stresses related to the alignment of muscular fibers in the external sphincter (**Choice A**).

(**Choice C**) Bilateral anal fissures are uncommon.

(**Choices D and E**) Fissures not at the midline are more likely due to unusual causes (eg, inflammatory bowel disease, malignancy, infection) and may warrant more detailed investigation.

**Educational objective:**



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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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exacerbating the constipation.

The majority of fissures, especially those causing prolonged symptoms, occur at the **posterior midline** of the anal verge. This is likely due to the relatively poor perfusion of the posterior anal canal, which makes its mucosa sensitive to trauma and slows healing times. Anterior midline fissures are less common, but may occur due to mechanical stresses related to the alignment of muscular fibers in the external sphincter **(Choice A)**.

**(Choice C)** Bilateral anal fissures are uncommon.

**(Choices D and E)** Fissures not at the midline are more likely due to unusual causes (eg, inflammatory bowel disease, malignancy, infection) and may warrant more detailed investigation.

### Educational objective:

Anal fissures are longitudinal tears in the mucosa. They are usually due to passage of hard stool in patients with chronic constipation. Most fissures occur at the posterior midline, likely due to decreased blood flow in this area. Fissures in other areas may be due to less common causes.

### References

- [Anorectal conditions: anal fissure and anorectal fistula.](#)



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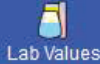
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Tutorial



Lab Values



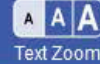
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Text Zoom



Settings

A 43-year-old obese woman presents to the emergency room with severe epigastric pain that started after a heavy meal. She has had several milder episodes before related to fatty food consumption. Physical examination reveals marked tenderness in the right subcostal area. Which of the following hormones most likely provoked the current attack in this patient?

- ☐ A. Secretin
- ☐ B. Cholecystokinin
- ☐ C. Gastrin
- ☐ D. Vasoactive intestinal peptide (VIP)
- ☐ E. Motilin
- ☐ F. Somatostatin

**Submit**

1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



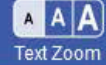
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 43-year-old obese woman presents to the emergency room with severe epigastric pain that started after a heavy meal. She has had several milder episodes before related to fatty food consumption. Physical examination reveals marked tenderness in the right subcostal area. Which of the following hormones most likely provoked the current attack in this patient?

- ☐ A. Secretin (2%)
- ☒ B. Cholecystokinin (89%)
- ☐ C. Gastrin (5%)
- ☐ D. Vasoactive intestinal peptide (VIP) (1%)
- ☐ E. Motilin (0%)
- ☐ F. Somatostatin (0%)

Correct



89%

Answered correctly



24 secs

Time Spent



08/27/2020

Last Updated

Block Time Remaining: 00:27:09

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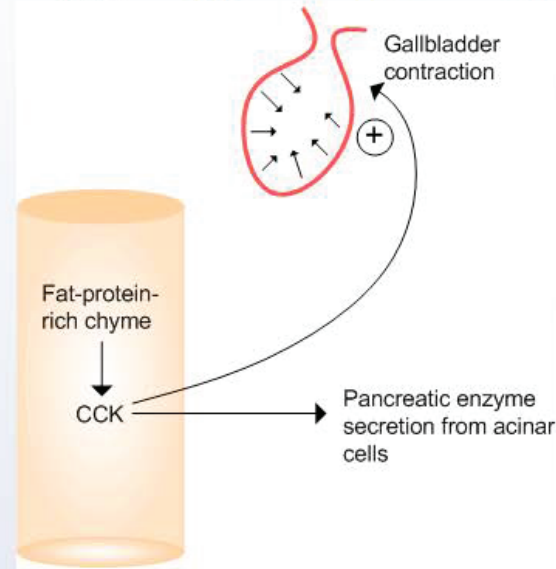


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This patient presents with classic signs and symptoms of biliary colic. Moreover, she has three well-known risk factors for gallbladder disease ("forty," "fat," and "female"). Cholecystokinin (CCK) is the hormone responsible for gallbladder contraction. It is produced by I cells of the duodenum and jejunum when fat-protein-rich chyme enters the duodenum. It functions to increase pancreatic enzyme secretion (by acinar cells) and gallbladder contraction, and to decrease gastric emptying. In cholecystitis, fatty foods increase CCK production and pain occurs when an inflamed and/or obstructed gallbladder contracts.



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

protein-rich chyme enters the duodenum. It functions to increase pancreatic enzyme secretion (by acinar cells) and gallbladder contraction, and to decrease gastric emptying. In cholecystitis, fatty foods increase CCK production and pain occurs when an inflamed and/or obstructed gallbladder contracts.

**(Choice A)** Secretin promotes bicarbonate secretion from pancreatic ductal epithelium. It has no effect on pancreatic enzyme secretion.

**(Choice C)** Gastrin is a hormone made in the stomach in response to stomach distention, peptides, and vagal stimulation. It stimulates gastric acid secretion and motility.

**(Choice D)** Vasoactive intestinal peptide (VIP) is produced in the pancreas and stimulates intestinal water secretion, counteracts gastrin in the stomach, and promotes bicarbonate secretion for the pancreas.

**(Choice E)** Motilin is a hormone made in the small intestine that promotes intestinal motility.

**(Choice F)** Somatostatin is a hormone made in numerous tissues (hypothalamus, stomach, intestine, pancreas) in response to low pH. Its production is inhibited by vagal stimulation. Somatostatin inhibits the release of growth hormone (GH) and thyroid stimulating hormone (TSH), and suppresses the release of myriad other molecules (e.g. gastrin, CCK, VIP, secretin, insulin, glucagon).

**Educational objective:**



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice C)** Gastrin is a hormone made in the stomach in response to stomach distention, peptides, and vagal stimulation. It stimulates gastric acid secretion and motility.

**(Choice D)** Vasoactive intestinal peptide (VIP) is produced in the pancreas and stimulates intestinal water secretion, counteracts gastrin in the stomach, and promotes bicarbonate secretion for the pancreas.

**(Choice E)** Motilin is a hormone made in the small intestine that promotes intestinal motility.

**(Choice F)** Somatostatin is a hormone made in numerous tissues (hypothalamus, stomach, intestine, pancreas) in response to low pH. Its production is inhibited by vagal stimulation. Somatostatin inhibits the release of growth hormone (GH) and thyroid stimulating hormone (TSH), and suppresses the release of myriad other molecules (e.g. gastrin, CCK, VIP, secretin, insulin, glucagon).

### Educational objective:

Cholecystikinin (CCK) is the hormone responsible for gallbladder contraction. It is made in the duodenum and jejunum in response to fatty acids and amino acids.

Physiology

Gastrointestinal &amp; Nutrition

Cholecystitis

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

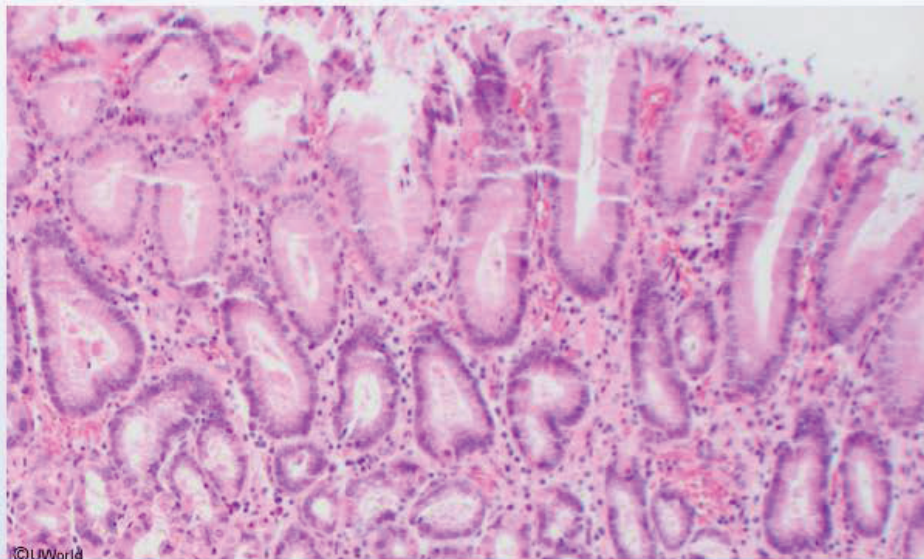


Text Zoom



Settings

A 2-year-old girl is brought to the emergency department with intermittent pain in the abdomen that began several hours ago. The patient also had a bowel movement that appeared tinged with blood. Ultrasound shows an area along the ileum in which the proximal small intestine is telescoped into the distal small intestine. Reduction via enema is unsuccessful, and the patient undergoes laparotomy with resultant resection of the involved intestine. The pathologic finding at the lead point is shown in the following image:



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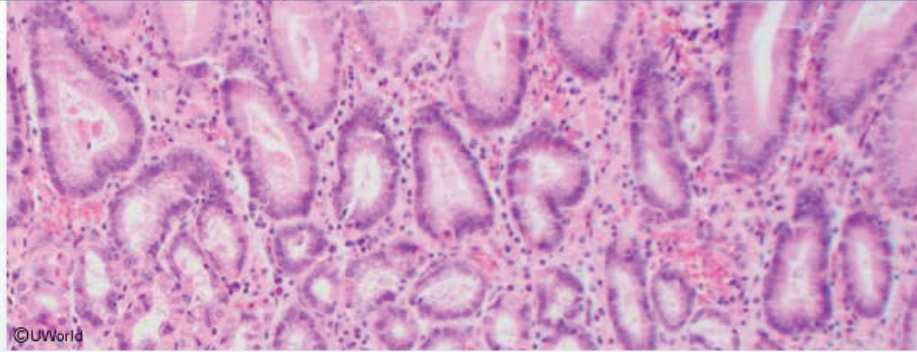
Feedback



Suspend

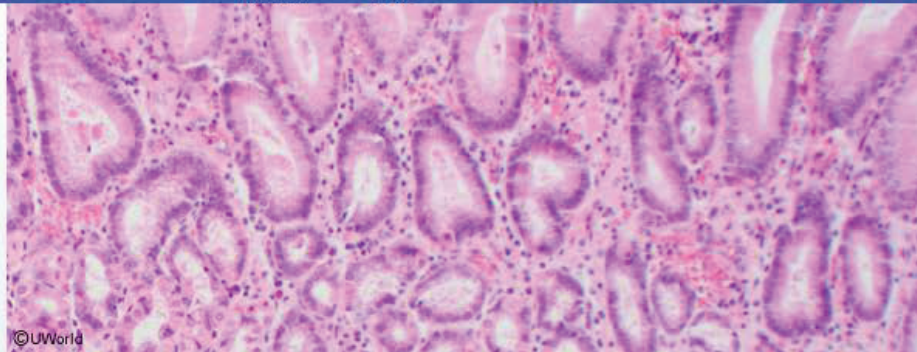


End Block



Which of the following is the most likely underlying diagnosis in this patient?

- ☐ A. Burkitt lymphoma
- ☐ B. Henoch-Schönlein purpura
- ☐ C. Inflammatory bowel disease
- ☐ D. Meckel diverticulum
- ☐ E. Pseudomembranous colitis



Which of the following is the most likely underlying diagnosis in this patient?

- ☐ A. Burkitt lymphoma (3%)
- ☐ B. Henoch-Schönlein purpura (13%)
- ☐ C. Inflammatory bowel disease (12%)
- ☒ D. Meckel diverticulum (67%)
- ☐ E. Pseudomembranous colitis (4%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

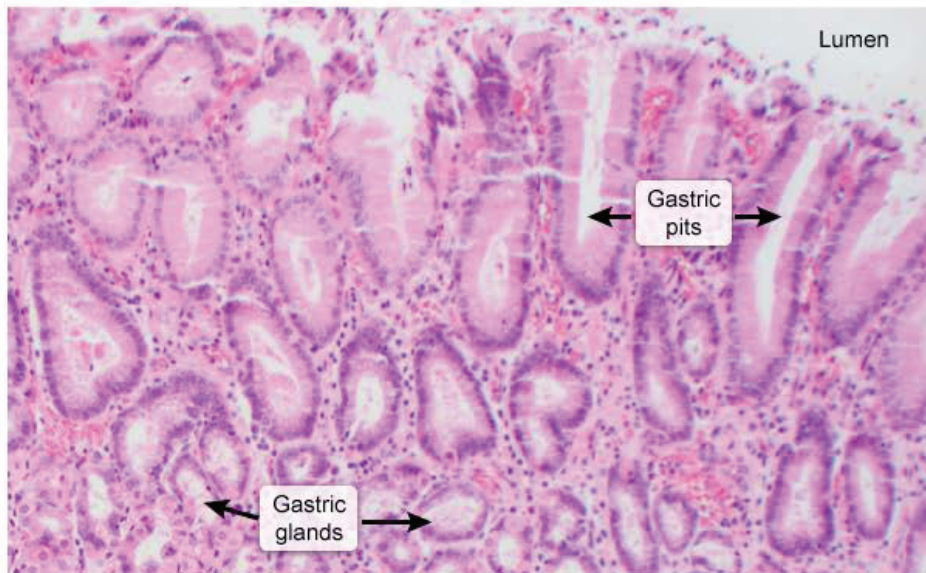


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Settings

### Normal gastric mucosa



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**Intussusception** occurs when a proximal segment of **intestine telescopes** into a distal segment, causing



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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**Intussusception** occurs when a proximal segment of **intestine telescopes** into a distal segment, causing episodes of severe abdominal pain. Progressive intestinal obstruction can also lead to bowel wall ischemia and bloody, currant jelly stools. Most cases are idiopathic in young children; however, 25% have a **pathologic lead point** for bowel invagination. The lead point is generally an anatomic abnormality (eg, polyp, mass) within the intestinal lumen that is entrapped during peristalsis and forced into distal bowel.

**Meckel diverticulum** is the **most common** pathologic lead point for intussusception and is a congenital anomaly of the gastrointestinal (GI) tract caused by incomplete obliteration of the **vitelline duct**. Most Meckel diverticula are clinically silent; symptomatic diverticula often contain **ectopic gastric mucosa**, which ulcerates and causes painless lower GI bleeding. Patients can also have complications such as diverticulitis, bowel obstruction, perforation, and intussusception.

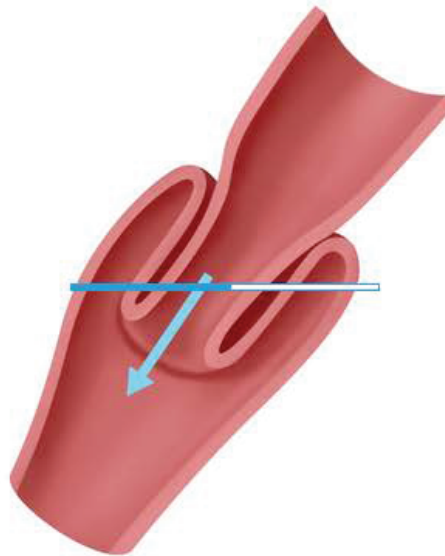
In some cases, Meckel diverticulum may be identified incidentally during laparotomy based on histologic evidence of gastric tissue within the small intestine. Distinct features of **gastric mucosa** include gastric glands and pits with chief cells and parietal cells. **Meckel scan** is a nuclear study that can be used to detect the presence of ectopic gastric mucosa and diagnose Meckel diverticulum.

**(Choice A)** **Burkitt lymphoma** can serve as a pathologic lead point for intussusception, but microscopy



Exhibit Display

Intussusception



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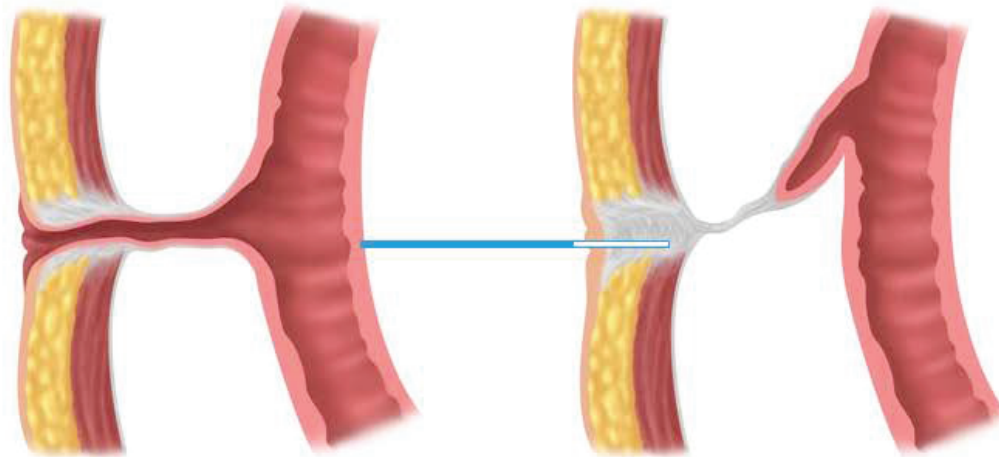
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Exhibit Display

### Vitelline duct abnormalities



Persistent vitelline duct

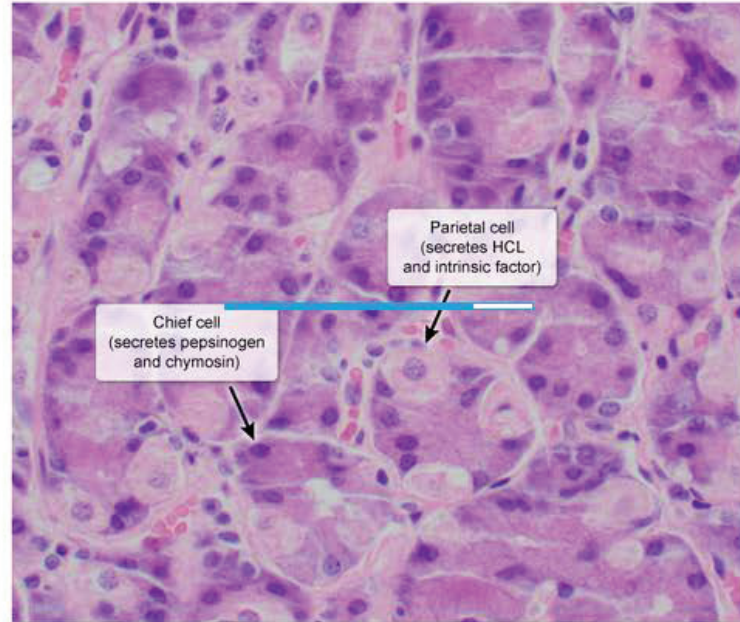
Meckel diverticulum

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Exhibit Display

Normal gastric mucosa



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Zoom In

Zoom Out

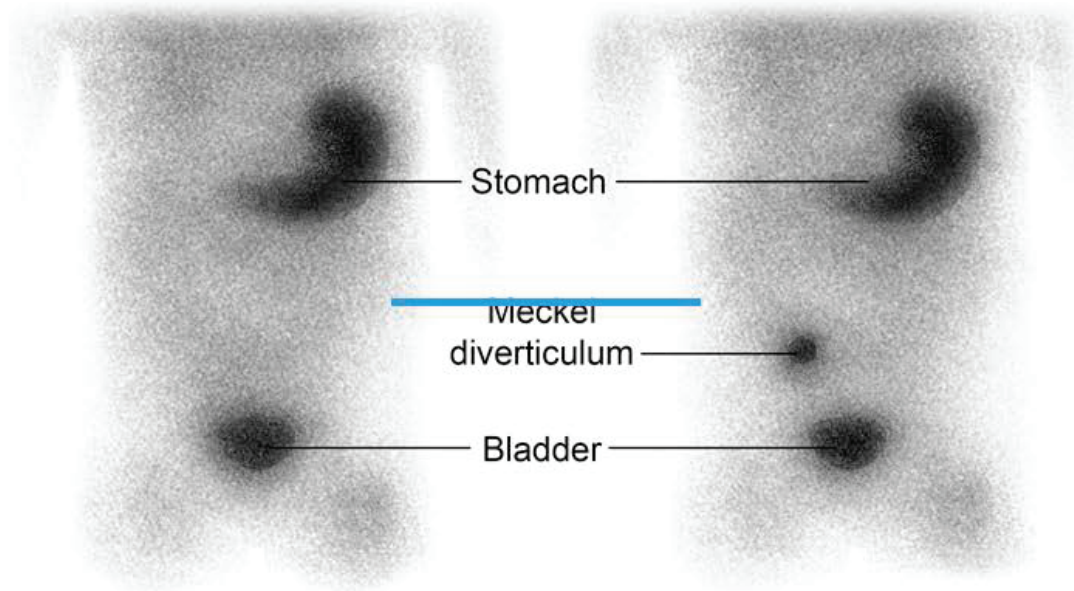
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Exhibit Display

# Meckel scan



Normal

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Reset

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**(Choice A)** Burkitt lymphoma can serve as a pathologic lead point for intussusception, but microscopy would show a lymphoid infiltrate in a starry sky pattern.

**(Choice B)** Intestinal edema and hemorrhage associated with Henoch-Schönlein purpura can trigger intussusception; however, leukocytoclastic vasculitis (perivascular neutrophils with fibrin deposits and nuclear debris) would be expected on microscopy.

**(Choices C and E)** Inflammatory bowel disease (eg, Crohn disease) and pseudomembranous colitis (ie, *Clostridioides difficile* infection) cause GI tract inflammation that could trigger intussusception, but the incidence is rare, particularly in a child age 2. In addition, microscopic findings of Crohn disease include transmural inflammation with noncaseating granulomas, and pseudomembranous colitis is characterized by pseudomembranes composed of fibrin, neutrophils, and acellular debris.

### Educational objective:

Meckel diverticulum is the most common pathologic lead point for intussusception, a condition in which a portion of the intestine telescopes into itself. Meckel diverticula frequently contain ectopic gastric mucosa, which can aid in diagnosis.

### References

- Clinical characteristics of intussusception secondary to pathologic lead points in children: a single-





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

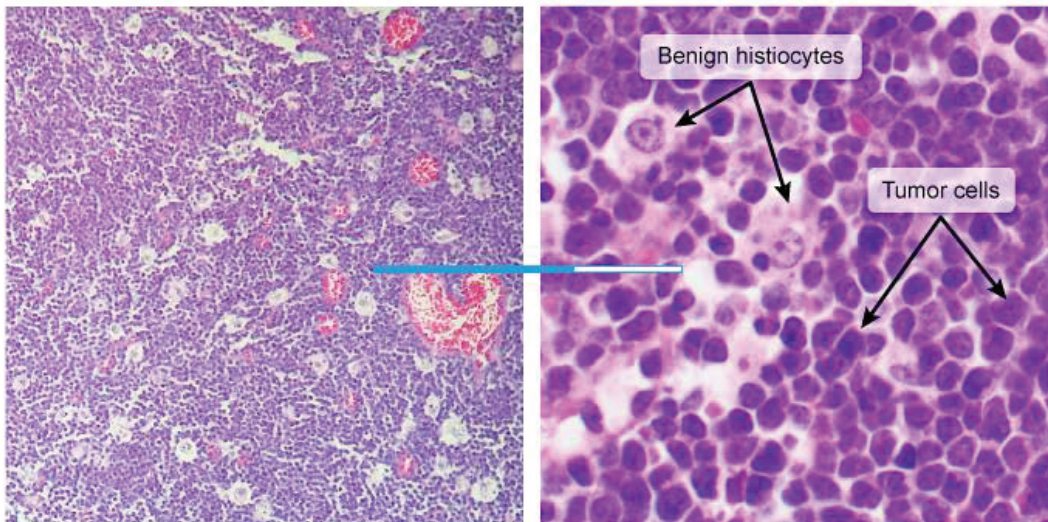
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(Choice A) Burkitt lymphoma can serve as a pathologic lead point for intussusception, but microscopy

## Exhibit Display

## Burkitt lymphoma



Lighter histiocytes in a field of darker tumor cells; "starry sky" appearance

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New | Existing

My Notebook



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Feedback



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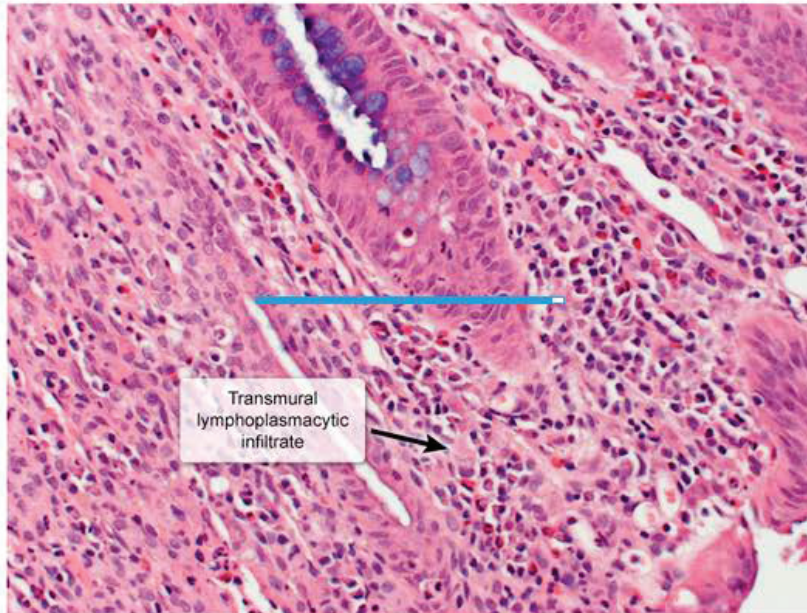
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(Choice A) Burkitt lymphoma can serve as a pathologic lead point for intussusception, but microscopy

## Exhibit Display

## Crohn disease



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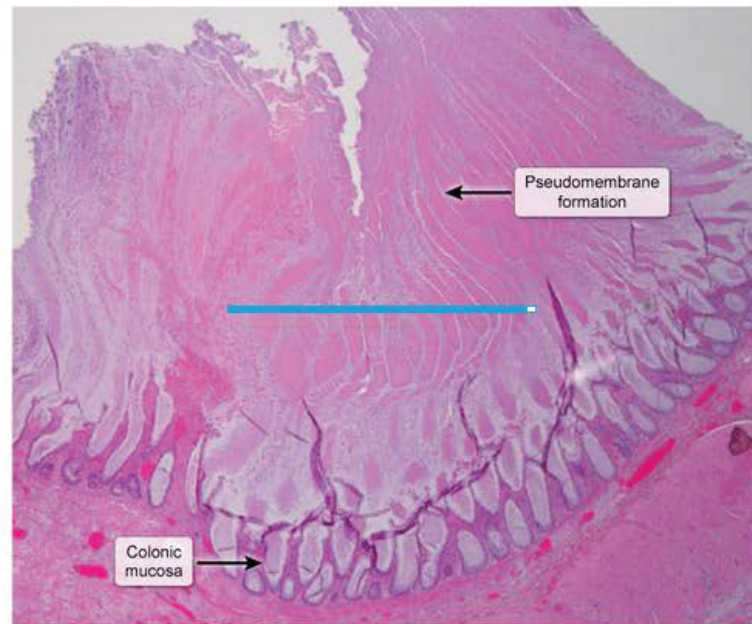
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(Choice A) Burkitt lymphoma can serve as a pathologic lead point for intussusception, but microscopy

## Exhibit Display

## Pseudomembranous colitis



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Zoom Out

Reset

New | Existing

My Notebook



A 62-year-old man comes to the emergency department due to acute-onset constipation. His last bowel movement was 4 days ago; before that time, his stools were always regular. Review of systems is positive for dry cough, increasing low back pain, a 9-kg (20-lb) weight loss in the past month, and increasing difficulty with urination. He has smoked 2 packs of cigarettes daily for 30 years. Vital signs are within normal limits. Point tenderness is elicited with palpation over the lower spine. Bilateral lower extremity weakness is present, and sensation is impaired in the perineal region. Chest x-ray reveals a right lung mass. Dysfunction of which of the following nerves best explains this patient's constipation?

- ☐ A. Greater splanchnic nerve
- ☐ B. Ilioinguinal nerve
- ☐ C. Lesser splanchnic nerve
- ☐ D. Pelvic splanchnic nerves
- ☐ E. Vagus nerve

**Submit**

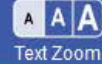
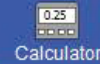
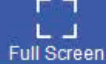


A 62-year-old man comes to the emergency department due to acute-onset constipation. His last bowel movement was 4 days ago; before that time, his stools were always regular. Review of systems is positive for dry cough, increasing low back pain, a 9-kg (20-lb) weight loss in the past month, and increasing difficulty with urination. He has smoked 2 packs of cigarettes daily for 30 years. Vital signs are within normal limits. Point tenderness is elicited with palpation over the lower spine. Bilateral lower extremity weakness is present, and sensation is impaired in the perineal region. Chest x-ray reveals a right lung mass. Dysfunction of which of the following nerves best explains this patient's constipation?

- ☐ A. Greater splanchnic nerve (4%)
- ☐ B. Ilioinguinal nerve (9%)
- ☐ C. Lesser splanchnic nerve (6%)
- ☒ D. Pelvic splanchnic nerves (63%)
- ☐ E. Vagus nerve (15%)







This patient with a lung mass has progressive low back pain, bilateral lower extremity weakness, bowel/bladder dysfunction, and impaired perineal sensation; this presentation is highly concerning for **cauda equina syndrome**. The **cauda equina** is formed from lumbosacral nerve roots which can be compressed by **epidural metastasis** (most commonly from lung cancer), trauma, or disc herniation. The symptoms of cauda equina syndrome result from disruption of nerve roots to the sciatic nerve (eg, lower extremity weakness, radicular low back pain), pudendal nerve (eg, saddle anesthesia), and/or pelvic splanchnic nerves.

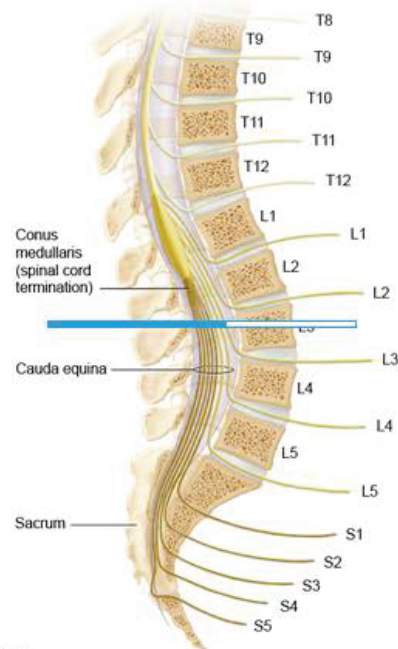
The **pelvic splanchnic nerves** (S2-S4) provide **parasympathetic** innervation to the hindgut, bladder, and urinary sphincters that promotes peristalsis, bladder emptying, and pelvic floor relaxation during defecation. **Constipation** and **difficulty urinating** are prominent symptoms in cauda equina syndrome due to loss of parasympathetic input to the bowel and bladder.

**(Choices A and C)** The greater splanchnic nerve (T5-T10) and lesser splanchnic nerve (T9-T12) provide sympathetic innervation to the foregut and midgut, respectively. In contrast to the parasympathetic nervous system, the sympathetic nervous system inhibits the gastrointestinal tract by slowing peristalsis. Disruption of these nerves can lead to increased gut motility, not constipation.



## Exhibit Display

## Relation of spinal nerve roots to vertebrae



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Zoom Out

Reset

New | Existing

My Notebook



**(Choice B)** The ilioinguinal nerve (L1) provides sensation to the superior medial thigh and part of the genitals, as well as motor innervation to the transverse abdominus and oblique abdominal musculature. Although it can be affected in cauda equina syndrome, it does not provide sympathetic or parasympathetic innervation to the gastrointestinal system.

**(Choice E)** The vagus nerve (CN X) originates in the medulla and provides parasympathetic innervation to the proximal gastrointestinal tract, ending at the level of the splenic flexure. Impairment of the vagus nerve is more likely to cause delayed gastric emptying and would not be caused by a lumbosacral spinal cord lesion.

### Educational objective:

The pelvic splanchnic nerves (S2-S4) provide parasympathetic innervation to the bowel and bladder, and their impairment in cauda equina syndrome can cause constipation and difficulty urinating. Other signs of cauda equina syndrome include radicular low back pain and leg weakness (sciatic nerve) as well as saddle anesthesia (pudendal, ilioinguinal nerves).

### References

- [Constipation in neurological diseases.](#)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 65-year-old man comes to the office after his wife insisted he get a checkup. The patient feels well and has no chronic medical conditions but has not seen a physician in many years. He received blood transfusions after a motor vehicle trauma in his 20s. The patient does not use tobacco or illicit drugs but drinks 2 or 3 alcoholic beverages daily. Physical examination reveals no hepatomegaly, ascites, or dilation of the superficial abdominal veins. The remainder of the examination shows no abnormalities. Serology is positive for hepatitis C antibodies. Chronic hepatitis C infection is confirmed with positive HCV RNA testing. After appropriate counseling is provided, combination therapy with sofosbuvir and ledipasvir is planned. This treatment is most likely to help clear the infection through which of the following mechanisms?

- ☐ A. Blocking reverse transcription of viral RNA
- ☐ B. Enhancing antiviral host immune response
- ☐ C. Impairing viral entry into host cells
- ☐ D. Inhibiting viral genome replication and assembly
- ☐ E. Preventing new virion release from infected host cells



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

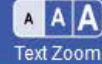
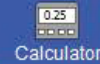
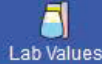
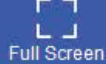
Text Zoom

Settings

has no chronic medical conditions but has not seen a physician in many years. He received blood transfusions after a motor vehicle trauma in his 20s. The patient does not use tobacco or illicit drugs but drinks 2 or 3 alcoholic beverages daily. Physical examination reveals no hepatomegaly, ascites, or dilation of the superficial abdominal veins. The remainder of the examination shows no abnormalities. Serology is positive for hepatitis C antibodies. Chronic hepatitis C infection is confirmed with positive HCV RNA testing. After appropriate counseling is provided, combination therapy with sofosbuvir and ledipasvir is planned. This treatment is most likely to help clear the infection through which of the following mechanisms?

- ☐ A. Blocking reverse transcription of viral RNA (16%)
- ☐ B. ~~Enhancing antiviral host immune response (3%)~~
- ☐ C. ~~Impairing viral entry into host cells (3%)~~
- ☒ D. Inhibiting viral genome replication and assembly (66%)
- ☐ E. Preventing new virion release from infected host cells (10%)





**Hepatitis C virus (HCV)** is a blood-borne pathogen that is primarily transmitted via injection drug use or transfusion of blood products (prior to widespread screening in 1992). Chronic infection develops in most individuals and increases the risk for cirrhosis and hepatocellular carcinoma. Because chronic HCV infection is often asymptomatic for decades, patients are often unaware that they have contracted the virus until they receive HCV screening.

Treatment of chronic HCV infection is with direct-acting antiviral (DAA) agents, which target specific enzymes in the HCV life cycle to **inhibit viral replication and assembly**, as follows:

- **RNA-dependent RNA polymerase inhibitors** – HCV binds to and enters host cells, uncoats, and subsequently replicates its genome using HCV-encoded RNA-dependent RNA polymerase. Nucleotide/non-nucleoside RNA polymerase inhibitors such as **sofosbuvir** target this step.
- **Protease inhibitors** – HCV mRNA is translated by host ribosomes into a polyprotein, which is cleaved by HCV protease into the individual proteins that compose the virus. HCV protease inhibitors such as **simeprevir** target this step.
- **NS5A inhibitors** – The HCV protein NS5A is crucial for viral replication and assembly (through unclear mechanisms) and is targeted by HCV medications such as **ledipasvir**.







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

- **NS5A inhibitors** – The HCV protein NS5A is crucial for viral replication and assembly (through unclear mechanisms) and is targeted by HCV medications such as **ledipasvir**.

DAA treatment results in a sustained virologic response (complete elimination of virus) in >97% of treated individuals.

**(Choice A)** HCV does not contain a reverse transcriptase enzyme so it does not integrate its genome into the host cell. Therefore, there are no reverse transcriptase inhibitors for HCV. Reverse transcriptase inhibitors are a mainstay of therapy for HIV.

**(Choice B)** Interferon-alpha was previously used in the treatment of chronic HCV (in combination with ribavirin) to trigger a broad antiviral immune response. However, interferon therapy has a lower cure rate (50%-80%) and a much higher incidence of side effects (eg, flu-like symptoms). Therefore, DAAs are now used preferentially.

**(Choice C)** HIV fusion inhibitors (eg, enfuvirtide) and CCR5 inhibitors (eg, maraviroc) inhibit the ability of HIV to enter cells. DAAs do not target viral entry.

**(Choice E)** Although HCV virion release could be a target for DAAs, there are currently no approved medications that target this step. Virion release (budding) is targeted by neuraminidase inhibitors in the



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice B)** Interferon-alpha was previously used in the treatment of chronic HCV (in combination with ribavirin) to trigger a broad antiviral immune response. However, interferon therapy has a lower cure rate (50%-80%) and a much higher incidence of side effects (eg, flu-like symptoms). Therefore, DAAs are now used preferentially.

**(Choice C)** HIV fusion inhibitors (eg, enfuvirtide) and CCR5 inhibitors (eg, maraviroc) inhibit the ability of HIV to enter cells. DAAs do not target viral entry.

**(Choice E)** Although HCV virion release could be a target for DAAs, there are currently no approved medications that target this step. Virion release (budding) is targeted by neuraminidase inhibitors in the treatment of influenza.

### Educational objective:

Chronic hepatitis C virus infection is treated with direct-acting antiviral (DAAs) medications such as ledipasvir and sofosbuvir. These medications target specific HCV enzymes (eg, protease, NS5A, RNA polymerase), which inhibits viral replication and assembly. Treatment with DAAs results in cure in >97% of patients.

### References

- HCV NS5A replication complex inhibitors



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 39-year-old woman is brought to the emergency department after an end-to-end motor vehicle collision. She was a restrained passenger and denies hitting her head or losing consciousness but has had abdominal pain and nausea since the accident. The patient's blood pressure is 115/55 mm Hg and pulse is 96/min and regular. On examination, she has ecchymosis over the area of the seat belt and abdominal tenderness. CT scan of the abdomen reveals a retroperitoneal hematoma. This patient most likely experienced which of the following injuries?

- ☐ A. Contusion of the body of the pancreas
- ☐ B. Laceration of the inferior border of the spleen
- ☐ C. Laceration of the right hepatic lobe
- ☐ D. Rupture of the suprarenal aorta
- ☐ E. Tear at the lesser curvature of the stomach
- ☐ F. Tear at the proximal transverse colon

**Submit**

Block Time Remaining: 00:29:15

TUTOR

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Feedback

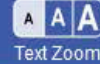
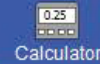
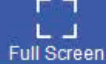


Suspend



End Block





A 39-year-old woman is brought to the emergency department after an end-to-end motor vehicle collision. She was a restrained passenger and denies hitting her head or losing consciousness but has had abdominal pain and nausea since the accident. The patient's blood pressure is 115/55 mm Hg and pulse is 96/min and regular. On examination, she has **ecchymosis** over the area of the seat belt and abdominal tenderness. CT scan of the abdomen reveals a **retroperitoneal hematoma**. This patient most likely experienced which of the following injuries?

- ☒ A. Contusion of the body of the pancreas (43%)
- ☐ B. Laceration of the inferior border of the spleen (38%)
- ☐ C. Laceration of the right hepatic lobe (2%)
- ☐ D. Rupture of the suprarenal aorta (12%)
- ☐ E. Tear at the lesser curvature of the stomach (0%)
- ☐ F. Tear at the proximal transverse colon (2%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Retroperitoneal abdominal organs

- Suprarenal (adrenal) glands
- Aorta & inferior vena cava
- Duodenum\* (except 1st part)
- Pancreas\* (head & body)
- Ureters
- Colon\* (ascending & descending)
- Kidneys
- Esophagus
- Rectum (mid-distal)

Mnemonic: **SAD PUCKER**

\*Secondarily retroperitoneal (developed intraperitoneal & migrated retroperitoneal).

**Retroperitoneal hematomas** are commonly associated with abdominal and pelvic trauma. Pancreatic injury is a frequent cause of retroperitoneal hematomas. It can occur following severe blunt or penetrating



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**Retroperitoneal hematomas** are commonly associated with abdominal and pelvic trauma. Pancreatic injury is a frequent cause of retroperitoneal hematomas. It can occur following severe blunt or penetrating abdominal trauma, such as from malpositioned seat belts or steering wheels during motor vehicle collisions. Pancreatic injury with retroperitoneal hematoma may initially cause only mild symptoms or be asymptomatic, but it can lead to life-threatening blood loss. Therefore, an abdominal CT scan is frequently performed in patients with blunt abdominal trauma to rule out retroperitoneal hematoma.

**(Choices B, C, E, and F)** The spleen, liver, stomach, and transverse colon are intraperitoneal organs. Lacerations or rupture of these organs can occur in blunt abdominal trauma, but these injuries would lead to hemoperitoneum (free blood in the peritoneal space), not retroperitoneal hematoma.

**(Choice D)** Although the abdominal aorta is a retroperitoneal structure, rupture would most likely result in massive and rapid blood loss leading to hemorrhagic shock.

### Educational objective:

Retroperitoneal hematoma is a common complication of abdominal and pelvic trauma. The pancreas is a retroperitoneal organ, and pancreatic injury is frequently a source of retroperitoneal bleeding.

### References

The diagnosis and treatment of traumatic retroperitoneal hematoma

Block Time Remaining: 00:30:05

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 55-year-old man comes to the office due to recurrent abdominal discomfort. He also has bloating, a feeling of fullness, and indigestion. Vital signs are within normal limits, and abdominal examination is unremarkable. Fecal occult blood testing is positive. Gastrointestinal endoscopic procedures are performed and confirm the presence of an ulcer. The patient is told that the ulcer itself is very unlikely to be malignant based on its location. Which of the following is the most likely site of this patient's gastrointestinal ulcer?

- ☐ A. Duodenum
- ☐ B. Esophagus
- ☐ C. Rectum
- ☐ D. Sigmoid colon
- ☐ E. Stomach

**Submit**

Block Time Remaining: 00:30:07

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Feedback



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom





Settings

A 55-year-old man comes to the office due to recurrent abdominal discomfort. He also has bloating, a feeling of fullness, and indigestion. Vital signs are within normal limits, and abdominal examination is unremarkable. Fecal occult blood testing is positive. Gastrointestinal endoscopic procedures are performed and confirm the presence of an ulcer. The patient is told that the ulcer itself is very unlikely to be malignant based on its location. Which of the following is the most likely site of this patient's gastrointestinal ulcer?

- ☒ A. Duodenum (80%)
- ☐ B. Esophagus (1%)
- ☐ C. Rectum (1%)
- ☐ D. Sigmoid colon (2%)
- ☐ E. Stomach (13%)

Correct

 80%  
Answered correctly 28 secs  
Time Spent 02/20/2021  
Last Updated

Block Time Remaining: 00:30:33

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Feedback



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



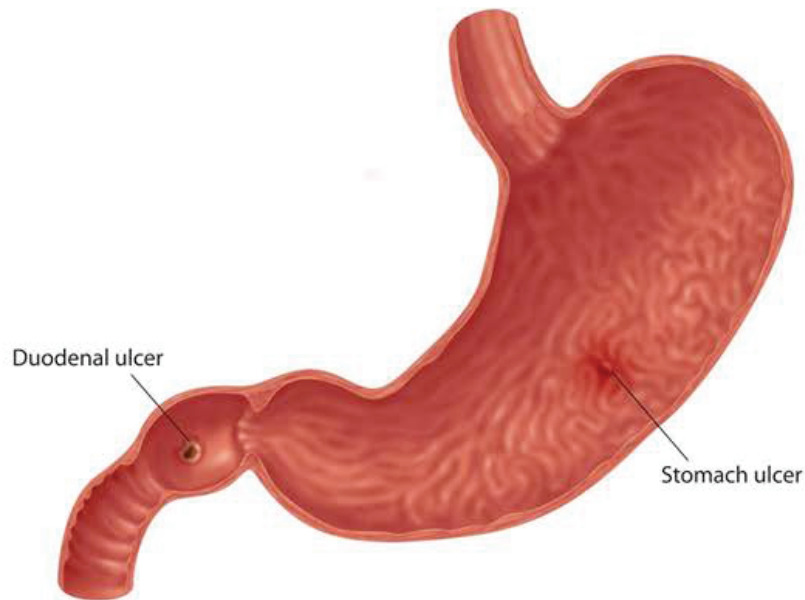
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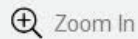
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## Exhibit Display

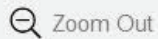
## Peptic ulcers



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Zoom In



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Feedback



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End Block



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39



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Gastrointestinal ulcers are defined as breaches of the alimentary tract mucosa that extend through the muscularis mucosae into the submucosa (or beyond). Those specifically designated as **peptic ulcers** are chronic lesions in areas exposed to acid/peptic juices, most commonly in the proximal duodenum, antral stomach, and gastroesophageal junction. Patients may present with epigastric discomfort, early satiety, and a positive fecal occult blood test.

Almost all peptic ulcers are due to either ***Helicobacter pylori*** infection or use of **nonsteroidal anti-inflammatory drugs (NSAIDs)**. The vast majority (>95%) of duodenal ulcers occur within the first part of the duodenum; however, multiple or refractory ulcers beyond the duodenal bulb may be seen in patients with gastrinoma (non-beta islet cell tumor of the pancreas). **Duodenal ulcers** are very **rarely malignant** and do not require biopsy. Conversely, gastric ulcers (located within the stomach) can be malignant (eg, gastric adenocarcinoma) and must be biopsied for confirmation (**Choice E**). Gastric ulcers caused by *H pylori* infection are associated with an increased risk of gastric cancer, but duodenal ulcers related to this infection do not lead to a higher risk of duodenal carcinoma.

**(Choice B)** Esophageal adenocarcinoma can appear as an ulcerated/exophytic lesion in the lower third of the esophagus and typically results from Barrett esophagus, chronic gastroesophageal reflux disease, obesity, and/or smoking. Esophageal squamous cell carcinoma appears as plaque-like thickening of the



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice B)** Esophageal adenocarcinoma can appear as an ulcerated/exophytic lesion in the lower third of the esophagus and typically results from Barrett esophagus, chronic gastroesophageal reflux disease, obesity, and/or smoking. Esophageal squamous cell carcinoma appears as plaque-like thickening of the mucosa in the upper two-thirds of the esophagus that may become ulcerated. Major risk factors include smoking, alcohol consumption, and caustic injury.

**(Choices C and D)** Carcinomas of the distal colon tend to be annular lesions that result in "napkin-ring" constriction of the bowel, with heaped-up edges and an ulcerated central region. Risk factors include advanced age, hereditary (eg, familial adenomatous polyposis) or sporadic colon cancer in the family, and inflammatory bowel disease.

### Educational objective:

Duodenal ulcers are not associated with an increased risk of carcinoma in the same location. In contrast, ulcers located in the esophagus, stomach (gastric), and colon may be malignant, and biopsy is required.

### References

- A past history of gastric ulcers and *Helicobacter pylori* infection increase the risk of gastric malignant lymphoma.
- The risk of gastric cancer in patients with duodenal and gastric ulcer: research progresses and clinical







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 15-year-old girl is hospitalized due to confusion and hematemesis for 2 days. Medical history is notable for depression over the past year. Temperature is 37.2 C (99 F), blood pressure is 86/56 mm Hg, pulse is 112/min, and respirations are 20/min; BMI is 23 kg/m<sup>2</sup>. She is oriented to person but disoriented to time and place. The patient quickly deteriorates and dies during hospitalization. Autopsy examination reveals a nodular liver, esophageal varices, splenomegaly, and atrophy of the basal ganglia with increased copper content. The most likely cause of this patient's condition is an abnormality in which of the following physiologic processes?

- ☐ A. Biliary excretion
- ☐ B. Immunoglobulin production
- ☐ C. Intestinal absorption
- ☐ D. Lipid metabolism
- ☐ E. Renal tubular reabsorption

**Submit**

Block Time Remaining: 00:30:34

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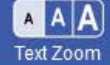
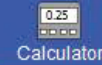
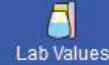
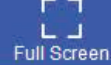


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A 15-year-old girl is hospitalized due to confusion and hematemesis for 2 days. Medical history is notable for depression over the past year. Temperature is 37.2 C (99 F), blood pressure is 86/56 mm Hg, pulse is 112/min, and respirations are 20/min; BMI is 23 kg/m<sup>2</sup>. She is oriented to person but disoriented to time and place. The patient quickly deteriorates and dies during hospitalization. Autopsy examination reveals a nodular liver, esophageal varices, splenomegaly, and atrophy of the basal ganglia with increased copper content. The most likely cause of this patient's condition is an abnormality in which of the following physiologic processes?

- ☒ A. Biliary excretion (56%)
- ☐ B. Immunoglobulin production (1%)
- ☐ C. Intestinal absorption (34%)
- ☐ D. Lipid metabolism (3%)
- ☐ E. Renal tubular reabsorption (3%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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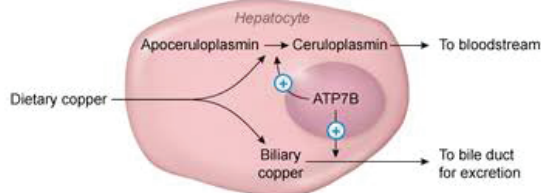


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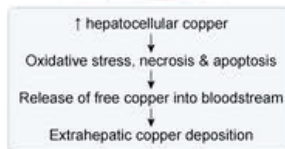
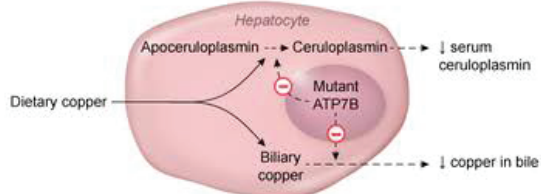
## Exhibit Display

## Copper metabolism and Wilson disease

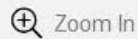
## Normal copper metabolism



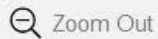
## Impaired copper metabolism in Wilson disease



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Feedback



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Previous



Next



Full Screen



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Notes



Calculator



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Text Zoom



Settings

This patient has evidence of **cirrhosis** (eg, nodular liver, splenomegaly, esophageal varices) with **acute liver failure** (ie, encephalopathy) in addition to copper deposition in the basal ganglia. These findings are consistent with **Wilson disease**, an autosomal recessive disorder characterized by accumulation of copper due to a **defective copper transport protein**, ATP7B.

In general, dietary copper is absorbed in the stomach and duodenum and bound to circulating albumin. It is then transported to the liver and taken up by hepatocytes. Excessive intracellular copper levels normally cause ATP7B to transfer the excess copper into the bile canaliculi. This process is essential for biliary excretion of copper, which accounts for the majority of total body copper excretion.

In Wilson disease, defective ATP7B results in **impaired biliary excretion** of copper. The **accumulation of hepatocellular copper** results in oxidative stress and apoptosis. Upon cell death, free copper is released into the bloodstream and **deposited into extrahepatic tissues** (eg, basal ganglia, cornea), causing the classic triad of hepatic, neurologic, and psychiatric (eg, depression) symptoms.

ATP7B is also required for the hepatic production of ceruloplasmin, which is apoceruloplasmin bound to copper. The inability to create and secrete ceruloplasmin in Wilson disease results in low serum ceruloplasmin. This abnormality does not account for the clinical manifestations of Wilson disease but is an important diagnostic finding.



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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

an important diagnostic finding.

**(Choice B)** Autoimmune hepatitis due to production of autoantibodies can cause cirrhosis and acute liver failure but not copper accumulation.

**(Choice C)** Hereditary hemochromatosis is an autosomal recessive disorder that can cause cirrhosis due to increased intestinal absorption of iron, not copper.

**(Choice D)** Niemann-Pick disease and Gaucher disease are lipid storage disorders that cause hepatosplenomegaly. Symptoms usually present in early childhood, and copper deposition is not seen in either condition.

**(Choice E)** Renal copper deposition in Wilson disease can cause Fanconi syndrome (eg, proximal tubular dysfunction). However, this occurs as a result of impaired biliary excretion of copper; it is not the cause of copper accumulation in Wilson disease.

### Educational objective:

Wilson disease is caused by defective copper transport within hepatocytes, which leads to impaired biliary excretion of copper. Hepatic copper accumulation eventually results in the release of free copper into the bloodstream and copper deposition into extrahepatic tissues (eg, basal ganglia, cornea).

### References

Block Time Remaining: 00:31:21

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Previous



Next



Full Screen



Tutorial



Lab Values



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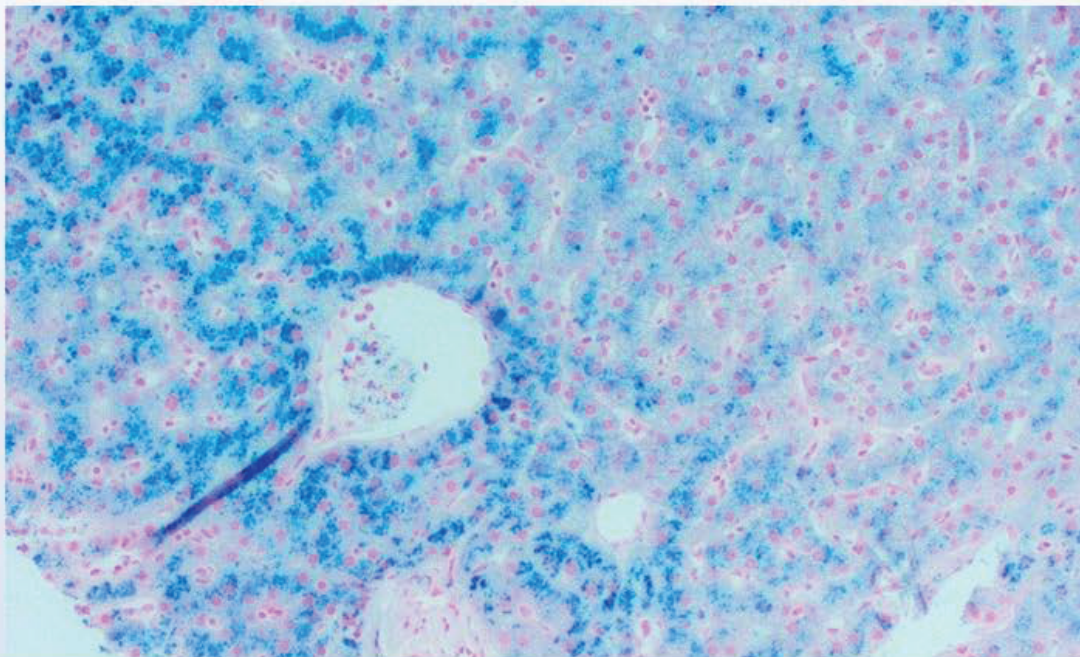


Text Zoom



Settings

A 63-year-old woman dies of congestive heart failure. Autopsy shows a dilated heart with brownish pigmentation of the myocardium. Light microscopy of her liver after Prussian blue staining is shown in the image below:



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Previous

Next



Full Screen



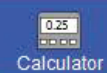
Tutorial



Lab Values



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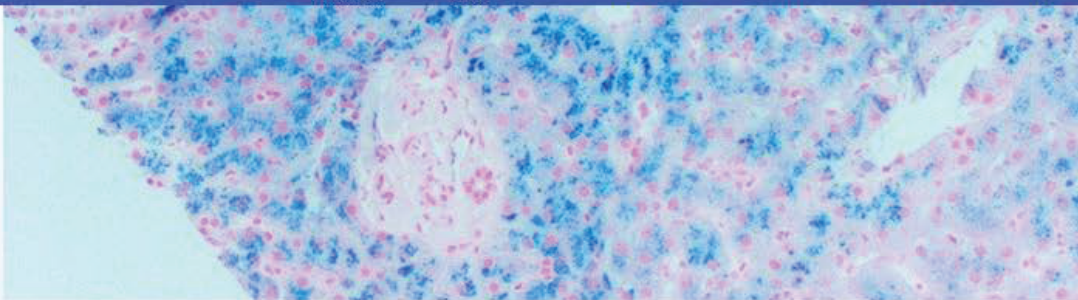
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Text Zoom



Settings



The patient's brother died of profuse upper gastrointestinal bleeding at age 43. Assuming this patient's disorder is hereditary, which of the following most likely contributed to the delayed onset of her disease compared to her brother?

- ☐ A. Heterozygosity for *HFE* gene mutation
- ☐ B. High-dose vitamin C intake
- ☐ C. Incomplete penetrance of homozygotic *HFE* mutations
- ☐ D. Premenopausal menstrual bleeding
- ☐ E. Receipt of blood transfusions



Feedback



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Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



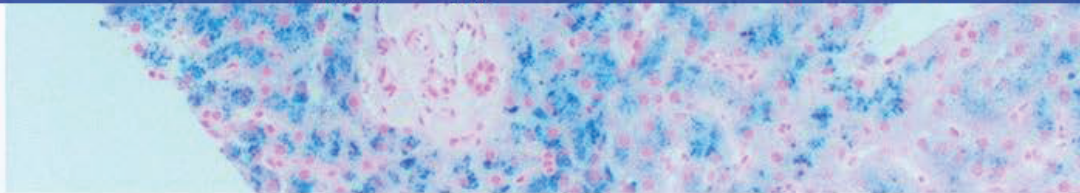
Reverse Color



Text Zoom



Settings



The patient's brother died of profuse upper gastrointestinal bleeding at age 43. Assuming this patient's disorder is hereditary, which of the following most likely contributed to the delayed onset of her disease compared to her brother?

- ☐ A. Heterozygosity for *HFE* gene mutation (11%)
- ☐ B. High-dose vitamin C intake (0%)
- ☐ C. Incomplete penetrance of homozygotic *HFE* mutations (14%)
- ☒ D. Premenopausal menstrual bleeding (72%)
- ☐ E. Receipt of blood transfusions (1%)

Correct

72%



39 secs



01/08/2021



Feedback

Suspend

End Block

<https://t.me/USMLEWorldStep1>



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



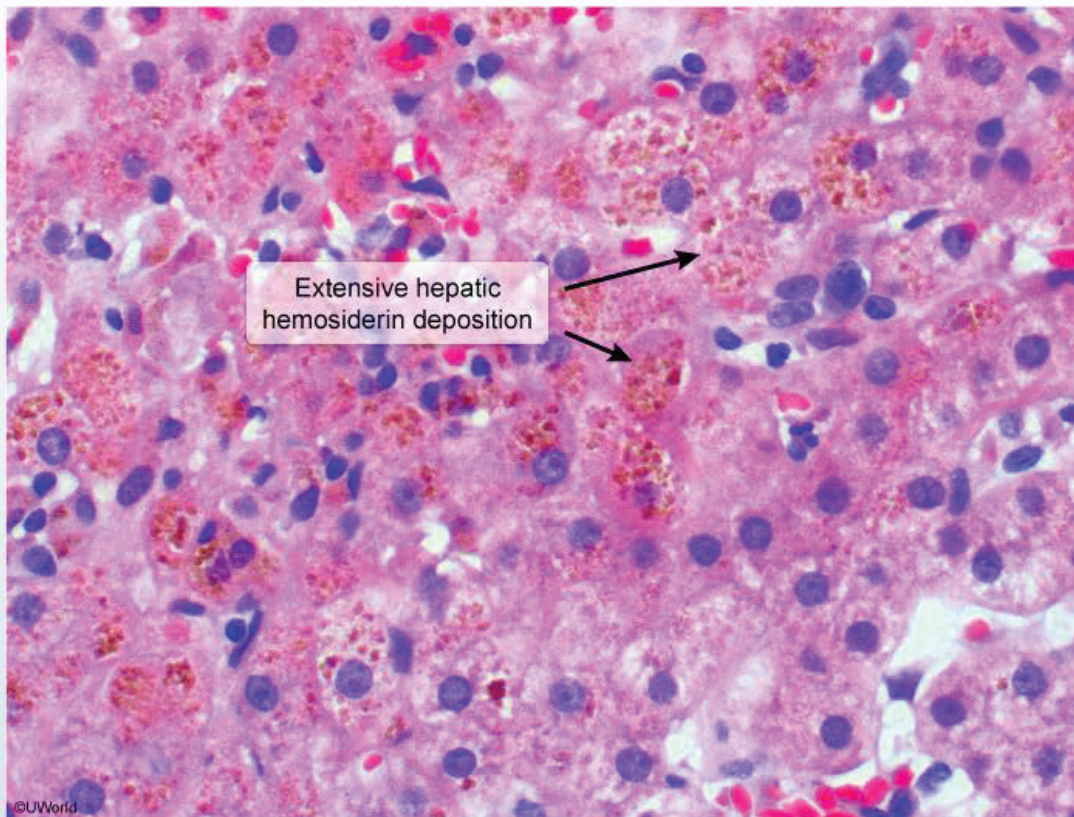
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Text Zoom



Settings



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Block Time Remaining: 00:32:00

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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This patient has cardiomyopathy with visible brown discoloration, which could represent lipofuscin (age-related pigment) or hemosiderin (iron deposition). However, her liver specimen shows diffuse infiltration of iron (visible as blue pigment granules after **Prussian blue** staining), confirming a diagnosis of iron overload. Given that her brother likely developed cirrhosis complicated by variceal hemorrhage in his 40s, the most probable underlying cause is **hereditary hemochromatosis (HH)**.

Total iron stores in the body are tightly regulated at the point of intake, with gastrointestinal absorption adjusted to match daily losses. HH is an autosomal recessive disorder characterized by **increased intestinal iron absorption**; because there is no specific mechanism to excrete unneeded iron, the excess iron (typically 0.5-1.0 g/yr) accumulates in the parenchymal organs (eg, liver, heart).

HH is usually silent in early adulthood, manifesting only after >20 g of iron has accumulated in the body. Men typically begin to develop symptoms in their 30s and 40s. However, **premenopausal women** have ongoing **blood (and iron) losses** due to **menstruation**, which partially offsets the excess iron absorption. Women therefore **develop manifestations later**, typically several years after menopause (ie, variable expressivity based on sex).

**(Choices A and C)** Most patients with HH have inactivating mutations in the *HFE* gene that cause impaired hepcidin secretion. Disease development requires biallelic genetic mutations (ie, affecting both



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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

ongoing **blood (and iron) losses** due to **menstruation**, which partially offsets the excess iron absorption.

Women therefore **develop manifestations later**, typically several years after menopause (ie, variable expressivity based on sex).

**(Choices A and C)** Most patients with HH have inactivating mutations in the *HFE* gene that cause impaired hepcidin secretion. Disease development requires biallelic genetic mutations (ie, affecting both alleles); heterozygotes are unaffected. Although biallelic *HFE* inactivation is necessary to develop the condition, most patients (>70%) with biallelic mutations never develop HH (ie, the disease exhibits incomplete penetrance) due to genetic and environmental modifiers. However, this patient developed HH manifestations at a typical age for women, which would not be explained by heterozygosity or incomplete penetrance.

**(Choice B)** Ascorbic acid (vitamin C) and citric acid enhance the absorption of inorganic iron in the gastrointestinal tract and therefore might lead to earlier disease manifestations instead of slowing its onset.

**(Choice E)** Frequent blood transfusions can also lead to iron overload and hemosiderosis (iron accumulation in parenchymal tissues). The opposite, therapeutic phlebotomy, is the preferred treatment for HH and has been shown to slow its progression.

**Educational objective:**

Block Time Remaining: 00:32:00

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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**(Choice B)** Ascorbic acid (vitamin C) and citric acid enhance the absorption of inorganic iron in the gastrointestinal tract and therefore might lead to earlier disease manifestations instead of slowing its onset.

**(Choice E)** Frequent blood transfusions can also lead to iron overload and hemosiderosis (iron accumulation in parenchymal tissues). The opposite, therapeutic phlebotomy, is the preferred treatment for HH and has been shown to slow its progression.

### Educational objective:

Hereditary hemochromatosis is characterized by increased intestinal iron absorption with deposition of excess iron in parenchymal tissues. Men typically develop manifestations in their 30s and 40s. However, premenopausal women have ongoing blood and iron losses due to menstruation, which partially offsets the excess iron absorption and delays the onset of symptoms.

Pathophysiology

Gastrointestinal &amp; Nutrition

Hemochromatosis

Subject

System

Topic

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Feedback



Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 32-year-old woman comes to the office due to postprandial abdominal pain and nausea. The patient has no diarrhea, constipation, bloody stools, or vomiting. Medical history is significant for rheumatoid arthritis. The abdomen is mildly tender to palpation at the epigastrium but without distension or hepatosplenomegaly. Laboratory studies reveal anemia. A small gastric ulcer is seen during upper endoscopy, and biopsies are negative for *Helicobacter pylori*. Biopsies of the duodenum reveal numerous intraepithelial lymphocytes, villous atrophy, and crypt hyperplasia. Based on these biopsy findings, this patient is at increased risk for developing which of the following conditions later in life?

- ☐ A. Angiodysplasia of the small bowel
- ☐ B. Colon adenocarcinoma
- ☐ C. Portal vein thrombosis
- ☐ D. Pyloric stenosis
- ☐ E. T-cell lymphoma

**Submit**

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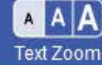
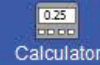
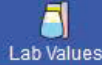
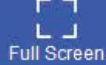


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A 32-year-old woman comes to the office due to postprandial abdominal pain and nausea. The patient has no diarrhea, constipation, bloody stools, or vomiting. Medical history is significant for rheumatoid arthritis. The abdomen is mildly tender to palpation at the epigastrium but without distension or hepatosplenomegaly. Laboratory studies reveal anemia. A small gastric ulcer is seen during upper endoscopy, and biopsies are negative for *Helicobacter pylori*. Biopsies of the duodenum reveal numerous intraepithelial lymphocytes, villous atrophy, and crypt hyperplasia. Based on these biopsy findings, this patient is at increased risk for developing which of the following conditions later in life?

- ☐ A. Angiodysplasia of the small bowel (9%)
- ☐ B. Colon adenocarcinoma (17%)
- ☐ C. Portal vein thrombosis (2%)
- ☐ D. Pyloric stenosis (4%)
- ☒ E. T-cell lymphoma (66%)





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Previous



Next



Full Screen



Tutorial



Lab Values



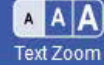
Notes



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Reverse Color



Text Zoom



Settings

### Celiac disease

<b>Pathogenesis</b>	<ul style="list-style-type: none"><li>• Gluten (gliadin) consumption → immune-mediated small intestine inflammation → chronic malabsorption</li></ul>
<b>Symptoms</b>	<ul style="list-style-type: none"><li>• Abdominal pain</li><li>• Diarrhea, flatulence &amp; bloating</li><li>• Failure to thrive (children) or weight loss</li><li>• Iron deficiency anemia</li><li>• Dermatitis herpetiformis</li></ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"><li>• Serology: tissue transglutaminase IgA, antiendomysial antibodies</li><li>• Duodenal biopsy: intraepithelial lymphocytes, villous atrophy, crypt hyperplasia</li></ul>
<b>Associated conditions</b>	<ul style="list-style-type: none"><li>• Autoimmune disorders (eg, type 1 diabetes)</li><li>• Cancer risk: T-cell lymphoma</li></ul>

This patient's presentation (abdominal pain, anemia) and biopsy findings are suggestive of **celiac disease**,



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient's presentation (abdominal pain, anemia) and biopsy findings are suggestive of **celiac disease**, an immune-mediated disorder triggered by gluten, a protein found in wheat, barley, and rye. Diarrhea is also common in celiac disease but may be absent.

Gliadin, a breakdown product of gluten, is primarily responsible for causing chronic inflammatory changes of the small bowel. Classic histologic findings, which are most prominent in the **proximal small bowel** (eg, duodenum, proximal jejunum), include intraepithelial lymphocytosis, **villous atrophy**, and crypt hyperplasia.

Chronic lymphocytic recruitment and proliferation within the small-bowel mucosa predisposes to **monoclonal T-cell expansion**, putting these patients at risk for enteropathy-associated **T-cell lymphoma**. This small-bowel cancer is usually very aggressive and has a poor prognosis despite chemotherapy.

**(Choice A)** Angiodysplasias are dilated, tortuous veins that develop in the gastrointestinal tract, most commonly in the small bowel and cecum. Risk factors include advanced age, chronic kidney disease, and aortic stenosis. They have no association with celiac disease.

**(Choice B)** In addition to small-bowel lymphoma, celiac disease is a risk factor for small-bowel adenocarcinoma. Unlike ulcerative colitis, familial adenomatous polyposis, and Lynch syndrome, celiac disease does not predispose to colon adenocarcinoma.



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Feedback



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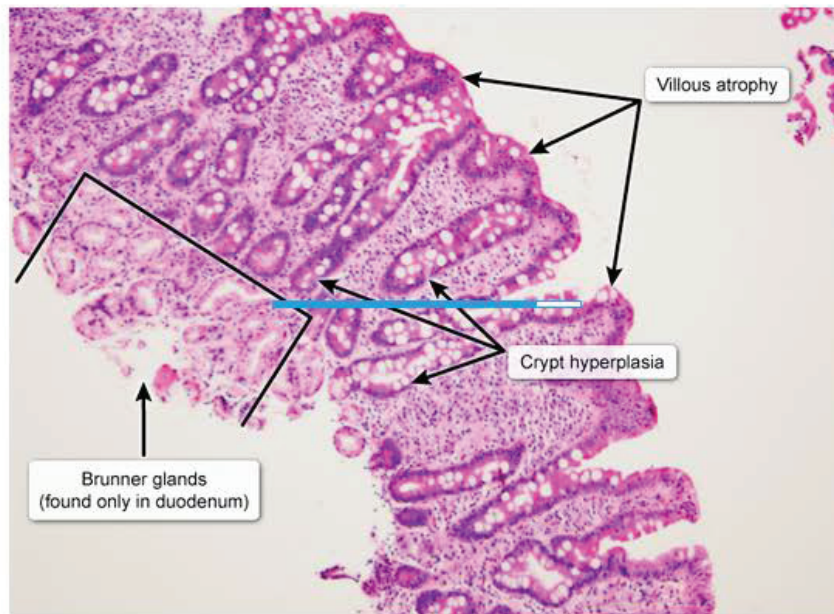
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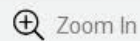
This patient's presentation (abdominal pain, anemia) and biopsy findings are suggestive of celiac disease

### Exhibit Display

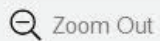
#### Celiac disease



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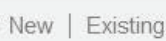
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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

aortic stenosis. They have no association with celiac disease.

**(Choice B)** In addition to small-bowel lymphoma, celiac disease is a risk factor for small-bowel adenocarcinoma. Unlike ulcerative colitis, familial adenomatous polyposis, and Lynch syndrome, celiac disease does not predispose to colon adenocarcinoma.

**(Choice C)** Portal vein thrombosis can create portal hypertension, predisposing to ascites and varices. This can occur in patients with hypercoagulable conditions such as polycythemia vera, as well as those with cirrhosis and hepatocellular carcinoma. Celiac disease does not predispose to portal vein thrombosis.

**(Choice D)** Pyloric stenosis is a congenital disorder that results from pyloric smooth muscle hypertrophy and typically presents with profuse vomiting in infants. It is not associated with celiac disease.

### Educational objective:

Celiac disease, an immune-mediated disorder triggered by gluten, causes small intestinal intraepithelial lymphocytosis, villous atrophy, and crypt hyperplasia. Monoclonal T-cell expansion can occur in the small-bowel mucosa of patients, leading to enteropathy-associated T-cell lymphoma.

Pathology

Gastrointestinal &amp; Nutrition

Celiac disease

Subject

System

Topic

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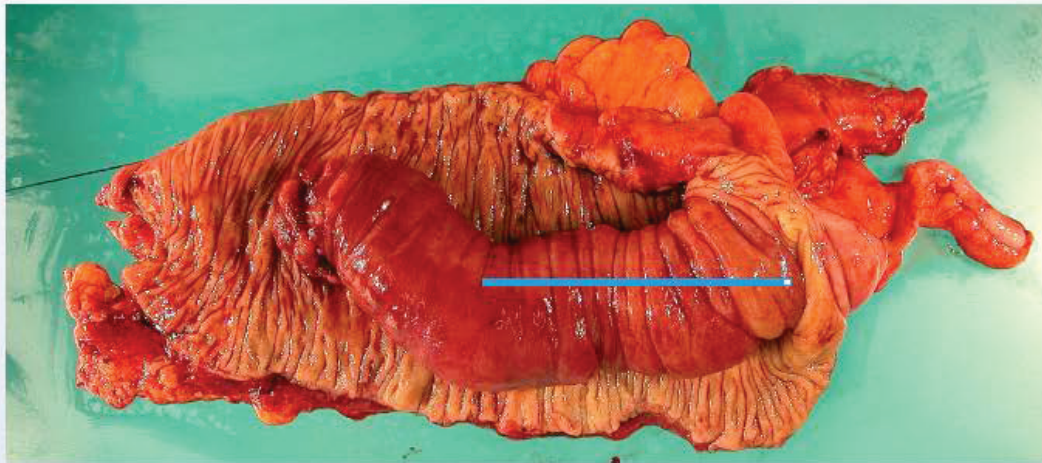


Suspend



End Block

A 2-year-old Caucasian boy is hospitalized with abdominal pain and vomiting. After initial evaluation laparotomy is performed, and a portion of the intestine is resected (see the slide below).



This patient most likely suffers from:

- ☐ A. Mesenteric adenitis
- ☐ B. Acute appendicitis





This patient most likely suffers from:

- ☐ A. Mesenteric adenitis
- ☐ B. Acute appendicitis
- ☐ C. Pseudomembranous colitis
- ☐ D. Ischemic colitis
- ☐ E. Collagenous colitis
- ☐ F. Intussusception
- ☐ G. Meckel diverticulitis





This patient most likely suffers from:

- ☐ A. Mesenteric adenitis (0%)
- ☐ B. Acute appendicitis (1%)
- ☐ C. Pseudomembranous colitis (0%)
- ☐ D. Ischemic colitis (2%)
- ☐ E. Collagenous colitis (0%)
- ☒ F. Intussusception (82%)
- ☐ G. Meckel diverticulitis (11%)

Correct

82%  
Answered correctly

17 secs  
Time Spent

01/30/2021  
Last Updated





This is a surgical specimen that has a portion of the intestine open with a necrotic segment found in the lumen. This is a typical picture of intussusception, an invagination of a portion of the intestine into the lumen of the adjacent intestinal segment (imagine a collapsed telescope). Intussusception leads to impaired venous return from the invaginated segment of the bowel, which can cause ischemia and subsequent necrosis of the intestinal wall.

The most typical location for intussusception is at the ileocolic junction. The size differences in the adjacent segments of the intestine allow the small bowel to invaginate into the cecum. Intussusception is most common in children younger than 2 years old. In this age group, it often occurs without any structural cause (sometimes associated with viral infection). In patients older than 2 years of age, a lead point, such as Meckel diverticulum, foreign body, or intestinal tumor, should be sought.

Clinical presentation is colicky, intermittent abdominal pain, nausea, vomiting, and "currant jelly" stools (that contain blood and mucus). A tubular mass may be palpable in the lower right abdominal quadrant. Barium enema is diagnostic and may be therapeutic. If the intussusception does not resolve with barium enema, surgical intervention is mandated.

### **Educational Objective:**

Intussusception most often occurs in children younger than 2 years of age and in the region of the ileocecal







segments of the intestine allow the small bowel to invaginate into the cecum. Intussusception is most common in children younger than 2 years old. In this age group, it often occurs without any structural cause (sometimes associated with viral infection). In patients older than 2 years of age, a lead point, such as Meckel diverticulum, foreign body, or intestinal tumor, should be sought.

Clinical presentation is colicky, intermittent abdominal pain, nausea, vomiting, and "currant jelly" stools (that contain blood and mucus). A tubular mass may be palpable in the lower right abdominal quadrant. Barium enema is diagnostic and may be therapeutic. If the intussusception does not resolve with barium enema, surgical intervention is mandated.

### Educational Objective:

Intussusception most often occurs in children younger than 2 years of age and in the region of the ileocecal valve. It manifests with intermittent, severe, colicky abdominal pain, "currant jelly" stools, and sometimes a palpable mass in the right lower abdominal quadrant.

Pathology

Gastrointestinal &amp; Nutrition

Intussusception

Subject

System

Topic

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Reverse Color



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A 39-year-old man comes to the clinic with a month-long history of fever, fatigue, joint pain, and an urticarial skin rash. He did not seek attention immediately as he hoped his symptoms would resolve. The patient is generally improving but is still very easily fatigued. Past medical history is unremarkable and the patient takes no regular medications, although he has not seen a physician since early childhood. He is not married and has a history of multiple heterosexual partners. The patient recently stopped smoking, drinks alcohol socially and does not use illicit drugs. Physical examination is notable for a moderately enlarged and tender liver. No jaundice is seen. Laboratory studies show significant elevations in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Which of the following is the most likely diagnosis in this patient?

- ☐ A. Acute hepatitis B
- ☐ B. Acute hepatitis C
- ☐ C. Gilbert syndrome
- ☐ D. Hemochromatosis
- ☐ E. Hepatic steatosis



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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Settings

skin rash. He did not seek attention immediately as he hoped his symptoms would resolve. The patient is generally improving but is still very easily fatigued. Past medical history is unremarkable and the patient takes no regular medications, although he has not seen a physician since early childhood. He is not married and has a history of multiple heterosexual partners. The patient recently stopped smoking, drinks alcohol socially and does not use illicit drugs. Physical examination is notable for a moderately enlarged and tender liver. No jaundice is seen. Laboratory studies show significant elevations in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Which of the following is the most likely diagnosis in this patient?

- ☐ A. Acute hepatitis B
- ☐ B. Acute hepatitis C
- ☐ C. Gilbert syndrome
- ☐ D. Hemochromatosis
- ☐ E. Hepatic steatosis
- ☐ F. Wilson disease



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takes no regular medications, although he has not seen a physician since early childhood. He is not married and has a history of multiple heterosexual partners. The patient recently stopped smoking, drinks alcohol socially and does not use illicit drugs. Physical examination is notable for a moderately enlarged and tender liver. No jaundice is seen. Laboratory studies show significant elevations in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Which of the following is the most likely diagnosis in this patient?

- ✓ ☒ A. Acute hepatitis B (70%)
- ☐ B. Acute hepatitis C (13%)
- ☐ C. Gilbert syndrome (2%)
- ☐ D. Hemochromatosis (7%)
- ☐ E. Hepatic steatosis (4%)
- ☐ F. Wilson disease (2%)

Correct

70%

01 min, 03 secs

02/05/2021



This patient has features of **acute hepatitis B** (HBV), including systemic, skin, and joint symptoms; hepatomegaly; and elevated transaminase levels. Hepatitis B is a DNA virus with an incubation period of 30-180 days. Transmission can occur sexually, parenterally, or vertically. Onset is dominated by nonspecific symptoms, although patients may develop a **serum sickness-like** syndrome with joint pain, lymphadenopathy, and a pruritic **urticarial vasculitis** rash. Right upper quadrant pain can also be present.

Acute HBV is characterized by significant elevations in **aspartate aminotransferase and alanine aminotransferase**, often >10 times the upper limit of normal. Most patients will have nonicteric hepatitis, but icteric hepatitis with jaundice and elevated bilirubin is also common. Impaired hepatic synthetic function, as indicated by a prolonged prothrombin time, confers a poor prognosis. The most important early marker of acute infection is **hepatitis B surface antigen** (HBsAg), which may be detectable prior to symptoms or changes in transaminase levels. IgM anti-hepatitis B core (anti-HBc) may also be positive. **Hepatitis B e antigen** (HBeAg) and HBV DNA counts correlate with **infectivity**.

**(Choice B)** Acute hepatitis C is typically asymptomatic; dermatologic manifestations (eg, cryoglobulinemia) are seen in chronic infection. This patient is unlikely to have hepatitis C as he does not use intravenous drugs and sexual transmission is rare.

**(Choice C)** Gilbert syndrome is a common disorder characterized by mild unconjugated





Item 2 of 40

Question Id: 365



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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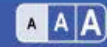


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End Block





**(Choice C)** Gilbert syndrome is a common disorder characterized by mild unconjugated hyperbilirubinemia. Patients are almost always asymptomatic.

**(Choice D)** Hemochromatosis is due to abnormal iron absorption resulting in iron overload. Chronic manifestations include cirrhosis, hyperpigmentation, and diabetes mellitus ("bronze diabetes").

**(Choice E)** Hepatic steatosis is characterized by excessive deposition of lipids in the liver and is usually caused by chronic alcohol abuse or obesity (and insulin resistance). Steatosis may lead to cirrhosis, but it does not cause acute symptoms.

**(Choice F)** Wilson disease presents with acute or chronic hepatitis in patients age <30. Neurologic manifestations (eg, cognitive or motor deficits) are frequent. Kayser-Fleischer rings (green or golden corneal deposits) are a common incidental finding.

### Educational objective:

Acute hepatitis B infection can cause a serum sickness-like syndrome with joint pain, lymphadenopathy, and a pruritic urticarial rash. Other features may include right upper quadrant pain, hepatomegaly, and elevated hepatic transaminase levels.

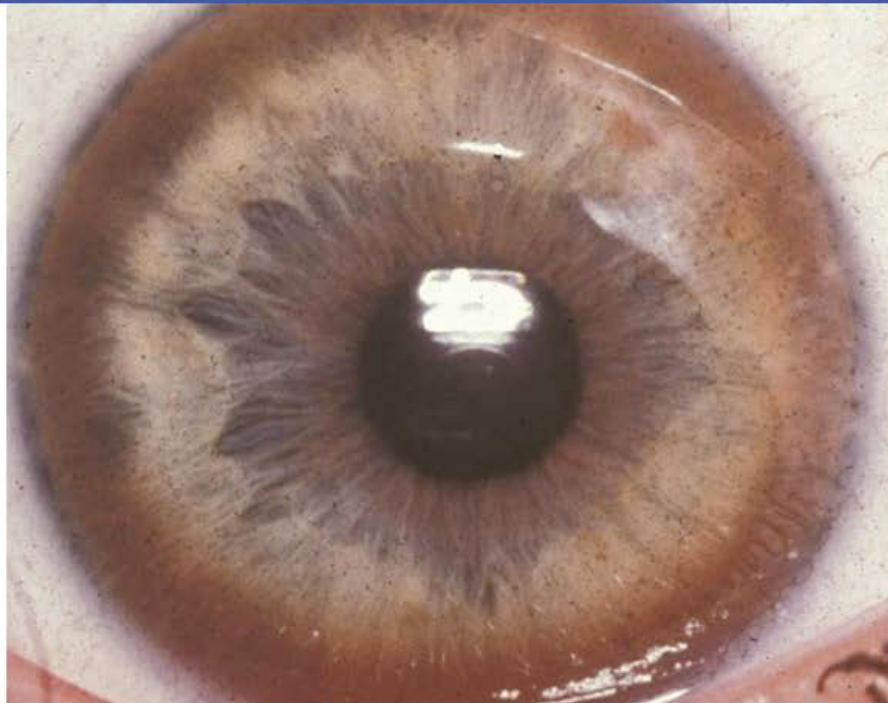
### References

- Cutaneous manifestations of viral hepatitis.



(Choice C) Gilbert syndrome is a common disorder characterized by mild unconjugated

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Cutaneous manifestations of viral hepatitis.

Block Time Remaining: 00:01:21

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A 42-year-old man comes to the office due to numbness and tingling in both legs and difficulty walking for the past several months. He has also noticed that he tires more easily with physical activity. His temperature is 36.8 C (98 F), blood pressure is 122/86 mm Hg, pulse is 76 /min, and respirations are 14/min. Physical examination shows conjunctival pallor and loss of vibration and position sensation in the bilateral lower extremities with associated gait ataxia. The remainder of the examination is within normal limits. Which of the following findings is most likely to be present upon further questioning of the patient?

- ☐ A. Ongoing treatment for latent tuberculosis
- ☐ B. Strict vegan diet for the past 6 years
- ☐ C. Total gastrectomy 8 months ago
- ☐ D. Use of an anti-epileptic drug for the past 3 months
- ☐ E. Working indoors most of the time

**Submit**





A 42-year-old man comes to the office due to numbness and tingling in both legs and difficulty walking for the past several months. He has also noticed that he tires more easily with physical activity. His temperature is 36.8 C (98 F), blood pressure is 122/86 mm Hg, pulse is 76 /min, and respirations are 14/min. Physical examination shows conjunctival pallor and loss of vibration and position sensation in the bilateral lower extremities with associated gait ataxia. The remainder of the examination is within normal limits. Which of the following findings is most likely to be present upon further questioning of the patient?

- ☐ A. Ongoing treatment for latent tuberculosis (5%)
- ✓ ☒ B. Strict vegan diet for the past 6 years (65%)
- ☐ C. Total gastrectomy 8 months ago (26%)
- ☐ D. Use of an anti-epileptic drug for the past 3 months (2%)
- ☐ E. Working indoors most of the time (0%)

Correct



65%

Answered correctly



45 secs

Time Spent



01/17/2021

Last Updated

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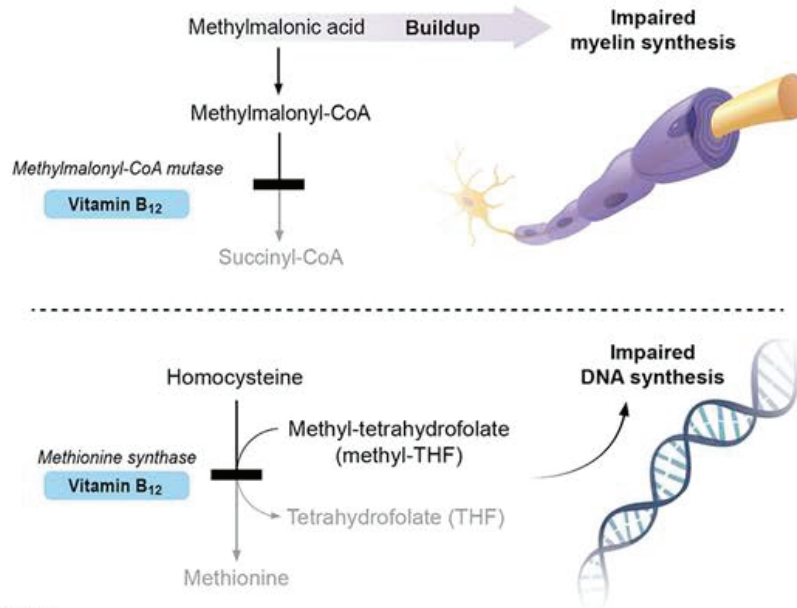
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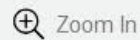
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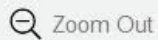
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Vitamin B<sub>12</sub> deficiency

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**Vitamin B12** (cobalamin) is obtained solely from the diet, specifically from **animal products** such as meat, dairy, and fish. Vitamin B<sub>12</sub> cannot be obtained from plant products, placing **strict vegans at risk for dietary deficiency**. The body is capable of storing about 1,000 times the daily requirement; therefore, vitamin B<sub>12</sub> deficiency develops only after the **complete absence of intake for 4-5 years**.

The development of **anemia** as well as severe and potentially irreversible neurologic damage can result from vitamin B<sub>12</sub> deficiency. Red blood cell synthesis relies on vitamin B<sub>12</sub>-dependent recycling of folate; deficiency of either vitamin results in a **megaloblastic anemia**. Neurologic symptoms vary in severity, but patients typically present with both motor and sensory deficits. Impaired myelin synthesis, specifically in the dorsal and lateral columns, results in **subacute combined degeneration of the spinal cord**. This condition is progressive and begins as a symmetrical neuropathy consisting of paresthesias and weakness. Ongoing deficiency leads to loss of vibration and position sensation with development of an ataxic gait. The longer the deficiency is untreated, the less likely it can be reversed.

**(Choice A)** Isoniazid, one of several drugs used to treat tuberculosis, may result in vitamin B<sub>6</sub> deficiency. Clinical manifestations consist of stomatitis, cheilosis, atrophic glossitis, sideroblastic anemia, and peripheral neuropathy. However, this patient's lack of oropharyngeal findings makes vitamin B<sub>6</sub> deficiency less likely.

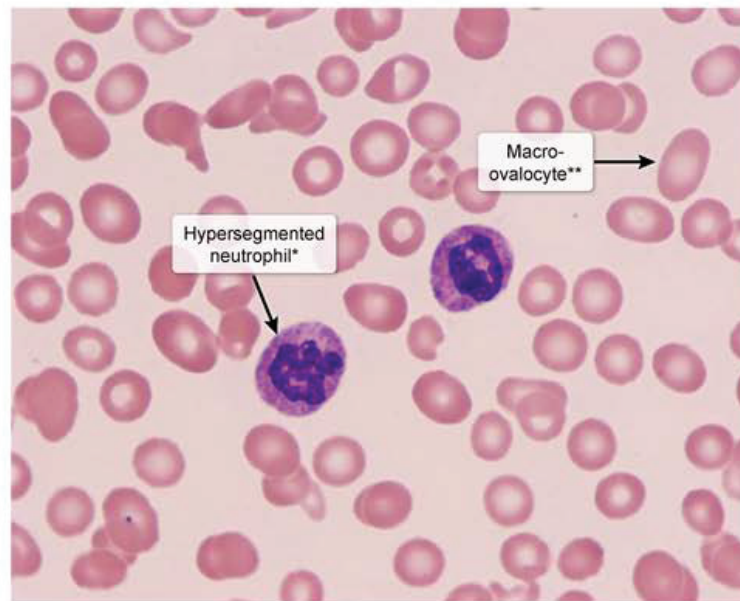






## Exhibit Display

## Megaloblastic anemia



Macro-ovalocyte\*\*

Hypersegmented neutrophil\*

\*≥ 6 nuclear lobes

\*\*Large, oval red blood cell

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less likely.

**(Choice C)** Patients undergoing total gastrectomy will inevitably develop B<sub>12</sub> deficiency if not given vitamin supplementation. However, this deficiency takes years to develop due to the large hepatic B<sub>12</sub> reserve, and would not occur after a period of only 8 months.

**(Choice D)** Phenytoin, an anti-epileptic drug used to treat both focal and generalized seizures, may result in folate deficiency and development of megaloblastic anemia. Phenytoin can also cause peripheral neuropathy, but this side effect usually only occurs with chronic therapy (>1 year).

**(Choice E)** Vitamin D deficiency can develop over the course of several months due to inadequate dietary intake and minimal sunlight exposure. This deficiency presents as rickets in children and osteomalacia or osteoporosis in adults.

**Educational objective:**

Vitamin B<sub>12</sub> is obtained through the diet solely from animal sources, which places strict vegans at risk for dietary deficiency. This deficiency takes years to develop due to the large hepatic B<sub>12</sub> reserve, and presents with megaloblastic anemia and potentially irreversible neurologic deficits (eg, paresthesias, weakness, ataxic gait).



A 65-year-old man comes to the office due to pain, redness, and swelling in his right calf. The patient is diagnosed with cellulitis and is started on clindamycin. A few days after starting treatment, he develops watery diarrhea and abdominal cramps. The patient is hospitalized, and complete blood count reveals leukocytosis. The toxin responsible for his current condition most directly impairs which of the following components of intestinal mucosal cells?

- ☐ A. Apical ion transport
- ☐ B. Cell membrane integrity
- ☐ C. Cytoskeleton integrity
- ☐ D. Mitochondrial energy production
- ☐ E. Ribosomal protein synthesis

Submit








A 65-year-old man comes to the office due to pain, redness, and swelling in his right calf. The patient is diagnosed with cellulitis and is started on clindamycin. A few days after starting treatment, he develops watery diarrhea and abdominal cramps. The patient is hospitalized, and complete blood count reveals leukocytosis. The toxin responsible for his current condition most directly impairs which of the following components of intestinal mucosal cells?

- ☐ A. Apical ion transport (23%)
- ☐ B. Cell membrane integrity (14%)
- ☒ C. Cytoskeleton integrity (53%)
- ☐ D. Mitochondrial energy production (0%)
- ☐ E. Ribosomal protein synthesis (7%)

Correct

 53%  
Answered correctly



01 min, 13 secs  
Time Spent



12/06/2020  
Last Updated



***Clostridioides difficile* colitis****Risk factors**

- Recent antibiotic use (eg, clindamycin)
- Hospitalization
- PPI

**Pathogenesis**

- Disruption of intestinal flora → *C. difficile* overgrowth
- Toxins A and B disrupt cytoskeleton integrity & stimulate inflammation

**Clinical presentation**

- Watery diarrhea (most common)
- Fulminant pseudomembranous colitis/toxic megacolon

**Diagnosis**

- Stool PCR for genes specific to toxigenic strains

**Treatment**

- Oral vancomycin OR fidaxomicin



**Treatment**

- Oral vancomycin OR fidaxomicin
- Metronidazole

**PCR** = polymerase chain reaction; **PPI** = proton pump inhibitor.

*Clostridioides* (formerly *Clostridium*) *difficile* is part of the gut's normal microbial flora in 2%-3% of healthy adults and in approximately 70% of healthy infants. Administration of **antibiotics** (eg, **clindamycin**, fluoroquinolones, and broad-spectrum penicillin) that are lethal to other commensal gut organisms can result in **C. difficile colitis** due to unchecked replication of pathogenic strains of *C. difficile*.

These strains produce **toxin A** and **toxin B**, which act synergistically, although toxin B is significantly more virulent. The toxins bind specific receptors on intestinal mucosal cells and are internalized, allowing them to inactivate Rho-regulatory proteins involved in actin cytoskeletal structure maintenance. The result is **loss of cytoskeleton integrity**, leading to cell rounding/retraction, disruption of intercellular tight junctions, and increased paracellular intestinal fluid secretion (eg, watery diarrhea). Both toxins also have **inflammatory effects** (eg, neutrophil recruitment) and can induce apoptosis, resulting in pain and **pseudomembrane** formation.

**(Choice A)** Apical ion transport is most directly affected by the cholera toxin (main exotoxin of *Vibrio*





inflammatory effects (eg, neutrophil recruitment) and can induce apoptosis, leading to pain and pseudomembrane formation.

**(Choice A)** Apical ion transport is most directly affected by the cholera toxin (main exotoxin of *Vibrio cholerae*) through activation of adenylate cyclase, which leads to decreased salt reabsorption and increased transport of sodium and chloride out of the gut mucosal cell. Apical ion transporters can be indirectly affected by *C. difficile* toxins due to loss of cell polarity (secondary to cytoskeletal dysfunction).

**(Choice B)** Loss of cell membrane integrity is characteristic of alpha toxin lecithinase, one of many exotoxins released by *Clostridium perfringens*. *C. perfringens* can cause transient watery diarrhea. However, it is most frequently associated with clostridial myonecrosis (ie, gas gangrene), a rapidly progressive form of fasciitis associated with penetrating injury by soil-contaminated objects.

**(Choice D)** Mitochondria are the primary source of ATP in human cells. Cyanide and nucleoside reverse transcriptase inhibitors are examples of drugs associated with mitochondrial toxicity.

**(Choice E)** Ribosomal protein synthesis is inhibited by shiga and shiga-like toxins. Shiga toxin is the main exotoxin released by *Shigella* species; shiga-like toxin (ie, verotoxin) is produced by enterohemorrhagic *Escherichia coli* (eg, O157:H7). These toxins cause inflammatory diarrhea (eg, fever, pain, blood) 3-4 days after ingestion of contaminated food or water.



However, it is most frequently associated with clostridial myonecrosis (ie, gas gangrene), a rapidly progressive form of fasciitis associated with penetrating injury by soil-contaminated objects.

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### Educational objective:

Pathogenic *Clostridioides difficile* can proliferate due to loss of commensal gut flora following use of broad-spectrum antibiotics (eg, clindamycin). *C. difficile* toxins A and B exert their effects by stimulating an inflammatory reaction and disrupting the actin cytoskeletal structure. The result is pseudomembranous colitis characterized by crampy abdominal pain, watery diarrhea, and leukocytosis.

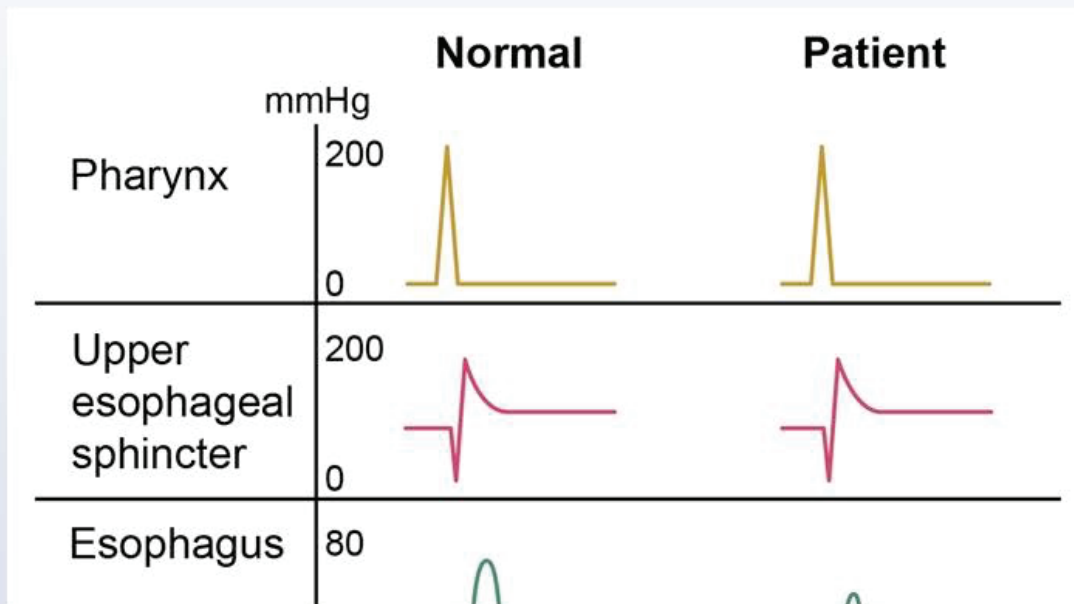
### References

- [The role of toxin A and toxin B in Clostridium difficile infection.](#)





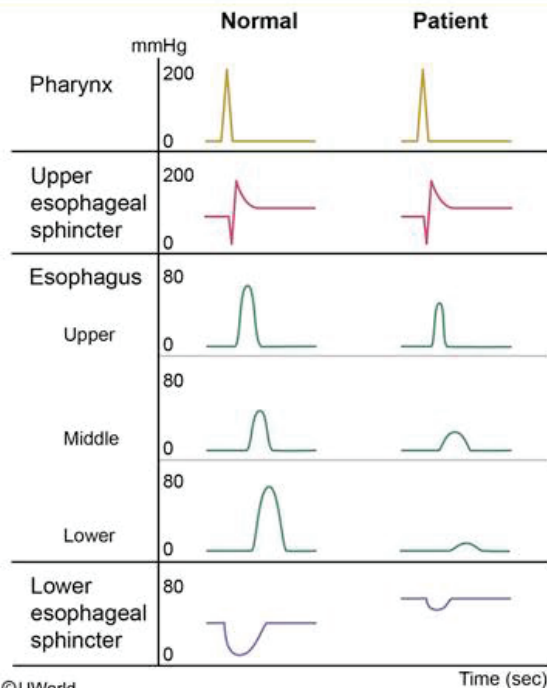
A 43-year-old man is evaluated for retrosternal discomfort and dysphagia for the past several months. He smokes a pack of cigarettes daily and drinks alcohol on weekends. His BMI is  $32.8 \text{ kg/m}^2$ . Physical examination is unremarkable. Esophageal manometry is performed; after a single swallow of 5 mL of water, the tracings appear as shown in the image below.







## Exhibit Display



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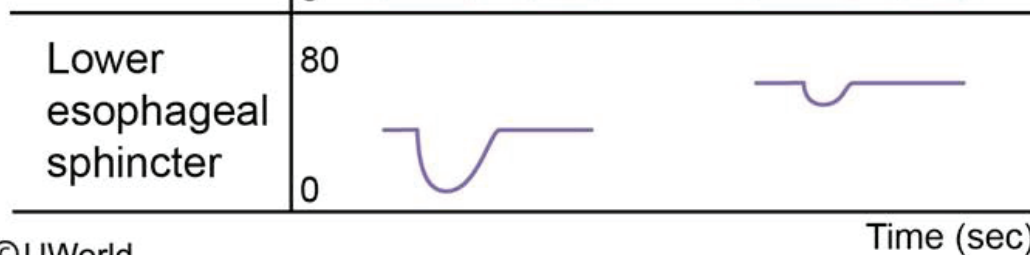
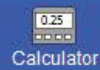
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Which of the following is the most likely diagnosis in this patient?

- ☐ A. Achalasia
- ☐ B. Cricopharyngeal dysfunction
- ☐ C. Diffuse esophageal spasm
- ☐ D. Esophageal stricture
- ☐ E. Systemic sclerosis

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Previous

Next

Full Screen

Tutorial

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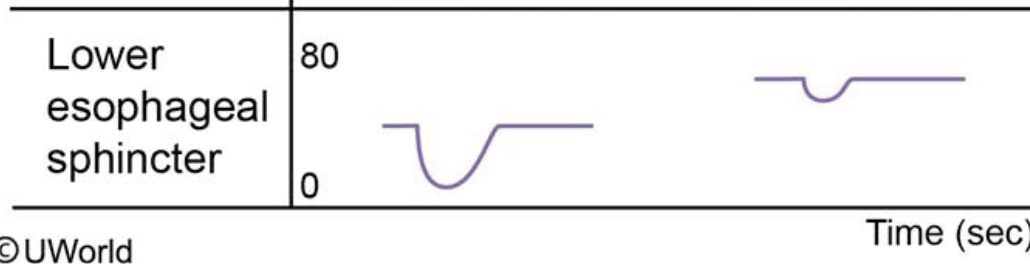
Notes

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Which of the following is the most likely diagnosis in this patient?

- ☒ A. Achalasia (74%)
- ☐ B. Cricopharyngeal dysfunction (1%)
- ☐ C. Diffuse esophageal spasm (4%)
- ☐ D. Esophageal stricture (9%)
- ☐ E. Systemic sclerosis (9%)

Correct

74%

30 secs

02/19/2021

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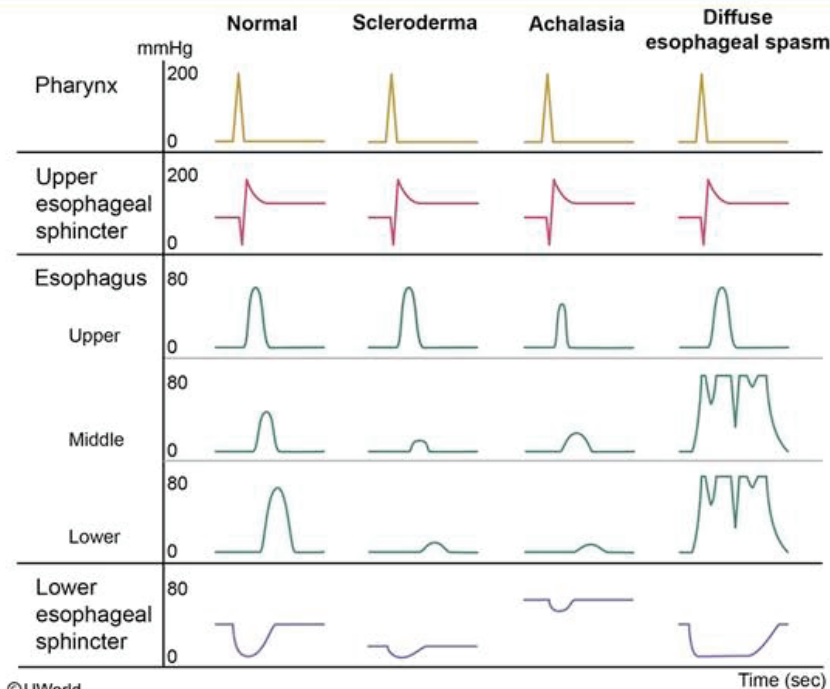
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To initiate swallowing, the contents of the oral cavity are collected on the tongue and propelled into the pharynx, where contraction of the pharyngeal muscles pushes the material into the esophagus. The cricopharyngeus muscle contracts behind the food bolus, initiating a peristaltic wave to propel the bolus downward. When the food bolus reaches the lower esophagus, the lower esophageal sphincter (LES) relaxes to allow the material to enter the stomach.

**Achalasia** is a motility disorder caused by reduced numbers of **inhibitory ganglion cells** in the esophageal wall, which creates an imbalance favoring excitatory ganglion cells. This patient's esophageal manometry shows typical findings in achalasia, including normal contraction of the upper esophageal sphincter, **decreased amplitude of peristalsis** in the mid esophagus, and increased tone and **incomplete relaxation** at the LES. Patients experience dysphagia, regurgitation, and retrosternal chest pain. **Barium esophagram** typically shows dilation of the esophagus with distal narrowing.

**(Choice B)** Cricopharyngeal dysfunction results from failure of the cricopharyngeus to relax during swallowing and causes a choking or "food-sticking" sensation on swallowing. Manometry findings are variable and can show decreased pharyngeal tone or incomplete relaxation at the upper esophageal sphincter.

**(Choice C)** Diffuse esophageal spasm presents with severe, retrosternal chest pain. It is characterized by





Item 5 of 40

Question Id: 828



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



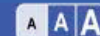
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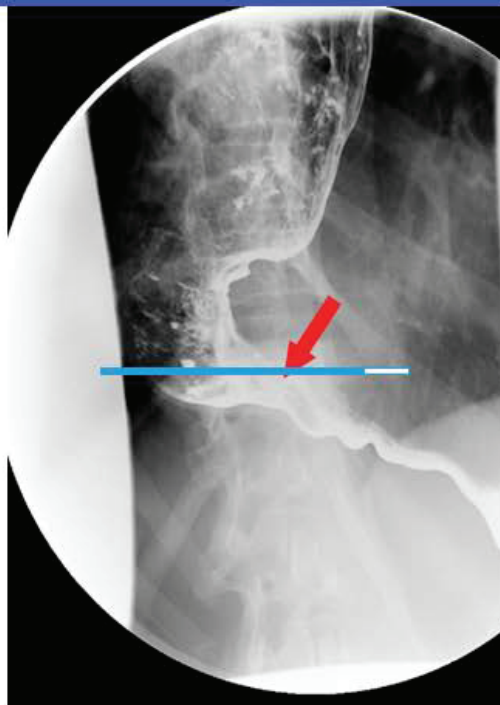


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(Choice C) Diffuse esophageal spasm presents with severe, retrosternal chest pain. It is characterized by

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Feedback



Suspend



End Block





**(Choice C)** Diffuse esophageal spasm presents with severe, retrosternal chest pain. It is characterized by uncoordinated contractions of the esophageal body. Esophageal manometry shows intermittent peristalsis and multiple simultaneous contractions on tracings from the mid and lower esophagus.

**(Choice D)** Esophageal stricture presents with progressive solid food dysphagia. It is diagnosed with contrast imaging (eg, barium swallow) rather than manometry. However, most patients will have a long history of gastroesophageal reflux with decreased tone at the LES.

**(Choice E)** Systemic sclerosis (scleroderma) can affect the esophagus, leading to impaired motility, incompetence of the LES, and gastroesophageal reflux. Manometry will show decreased peristalsis with decreased tone at the LES.

### Educational objective:

Achalasia is caused by reduced numbers of inhibitory ganglion cells in the esophageal wall. Esophageal manometry in achalasia shows decreased amplitude of peristalsis in the mid esophagus, with increased tone and incomplete relaxation at the lower esophageal sphincter.

Pathophysiology

Gastrointestinal &amp; Nutrition

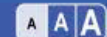
Achalasia

Subject

System

Topic





A 68-year-old man comes to the office due to fatigue, weight loss, and constipation. He has refused to undergo screening colonoscopy for several years because "nobody in my family had colon cancers." Past medical history is notable for emphysema and stable angina. The patient has smoked a pack of cigarettes daily for 50 years and drinks alcohol occasionally. Physical examination is unremarkable. He is referred for colonoscopy, which reveals a circumferential mass encircling the sigmoid colon. Pathology is positive for adenocarcinoma. CT scan of the chest, abdomen, and pelvis is negative for signs of metastasis. Serum carcinoembryonic antigen assay is ordered. The results of this assay would be most useful for which of the following aspects of this patient's care?

- ☐ A. Determining the need for surgery
- ☒ B. Determining the type of chemotherapy
- ☐ C. Grading of the tumor
- ☐ D. Monitoring for residual disease
- ☐ E. Staging of the tumor





undergo screening colonoscopy for several years because "nobody in my family had colon cancers." Past medical history is notable for emphysema and stable angina. The patient has smoked a pack of cigarettes daily for 50 years and drinks alcohol occasionally. Physical examination is unremarkable. He is referred for colonoscopy, which reveals a **circumferential mass encircling** the sigmoid colon. Pathology is positive for **adenocarcinoma**. CT scan of the chest, abdomen, and pelvis is negative for signs of metastasis. Serum carcinoembryonic antigen assay is ordered. The results of this assay would be most useful for which of the following aspects of this patient's care?

- ☐ A. Determining the need for surgery (1%)
- ☐ B. Determining the type of chemotherapy (8%)
- ☐ C. Grading of the tumor (3%)
- ☒ D. Monitoring for residual disease (80%)
- ☐ E. Staging of the tumor (5%)

Correct



80%

Answered correctly



01 min, 07 secs

Time spent



10/13/2020

Last updated

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**Carcinoembryonic antigen (CEA)** is a glycoprotein involved in cell adhesion. It is produced in the embryonic pancreas, liver, and intestine and is also detected in minute amounts in the serum of healthy adults. CEA levels are increased in most patients with colon cancer. Elevated **preoperative CEA** levels are associated with a worse **prognosis**, and failure to normalize following surgery suggests **residual disease**. During long-term follow-up, rising CEA levels are a sensitive indicator of colorectal cancer **recurrence**. However, CEA has low sensitivity and specificity for initial screening and diagnosis of colon cancer.

CEA levels are elevated in pancreatic, gastric, and breast malignancies along with other nonmalignant diseases (eg, inflammatory bowel disease, chronic obstructive pulmonary disease, cirrhosis, pancreatitis). CEA levels are also higher in smokers than nonsmokers.

**(Choice A)** Surgical resection is recommended for most patients with colon cancer unless there are unresectable metastases. The specific procedure recommended is dependent on stage and anatomical considerations rather than CEA levels.

**(Choice B)** Adjuvant chemotherapy is recommended for most patients with node-positive colorectal adenocarcinoma regardless of CEA levels.

**(Choices C and E)** Tumor grade describes the degree of tumor differentiation and is determined





**(Choice B)** Adjuvant chemotherapy is recommended for most patients with node-positive colorectal adenocarcinoma regardless of CEA levels.

**(Choices C and E)** Tumor grade describes the degree of tumor differentiation and is determined histologically. The stage of the tumor reflects the extent of its spread (eg, penetration of the bowel wall, lymph node invasion, distant metastases). Elevated CEA levels are associated with a worse prognosis regardless of tumor stage, but CEA measurement is not currently considered part of the initial staging evaluation.

### Educational objective:

Carcinoembryonic antigen (CEA) levels are increased in colon cancer but are also elevated in a number of other conditions (eg, pancreatic cancer, COPD, cirrhosis). CEA cannot be used to diagnose colon cancer, but it is helpful for detecting residual disease and recurrence.

### References

- [Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer.](#)

Pathology

Gastrointestinal &amp; Nutrition

Colorectal polyps and cancer

Subject

System

Topic



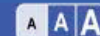


A 3-day-old girl is brought to the emergency department by her parents due to persistent vomiting and refusal to feed. The vomiting began early in the morning and has been a greenish-yellow color. The emesis does not contain blood. The infant appears dehydrated. Her heart rate is 175/min and blood pressure is within normal limits. After initial evaluation is complete, the infant undergoes laparotomy. Findings include a normal-appearing duodenum, the absence of a large segment of jejunum and ileum, and the remainder of the distal ileum winding around a thin vascular stalk. Which of the following intrauterine processes is most likely responsible for this patient's condition?

- ☐ A. Abnormal rotation
- ☐ B. Cell migration failure
- ☐ C. Failure of partitioning
- ☐ D. Recanalization failure
- ☐ E. Vascular occlusion

**Submit**





A 3-day-old girl is brought to the emergency department by her parents due to persistent vomiting and refusal to feed. The vomiting began early in the morning and has been a greenish-yellow color. The emesis does not contain blood. The infant appears dehydrated. Her heart rate is 175/min and blood pressure is within normal limits. After initial evaluation is complete, the infant undergoes laparotomy. Findings include a normal-appearing duodenum, the absence of a large segment of jejunum and ileum, and the remainder of the distal ileum winding around a thin vascular stalk. Which of the following intrauterine processes is most likely responsible for this patient's condition?

- ☐ A. Abnormal rotation (32%)
- ☐ B. Cell migration failure (11%)
- ☐ C. Failure of partitioning (5%)
- ☐ D. Recanalization failure (21%)
- ☒ E. Vascular occlusion (28%)





### Intestinal atresias

	Duodenal	Jejunum/Ileum	Colonic
Pathophysiology	<ul style="list-style-type: none"><li>• Failure of recanalization at 8-10 weeks gestation</li></ul>	<ul style="list-style-type: none"><li>• Vascular injury</li></ul>	<ul style="list-style-type: none"><li>• Unknown</li></ul>
Clinical findings	<ul style="list-style-type: none"><li>• Bilious or nonbilious emesis</li><li>• <b>Double-bubble</b> sign on x-ray</li></ul>	<ul style="list-style-type: none"><li>• <b>Bilious</b> emesis</li><li>• Abdominal distension</li></ul>	<ul style="list-style-type: none"><li>• Constipation</li><li>• Abdominal distension</li></ul>
Associations	<ul style="list-style-type: none"><li>• <b>Down syndrome</b></li></ul>	<ul style="list-style-type: none"><li>• Gastroschisis</li></ul>	<ul style="list-style-type: none"><li>• Hirschsprung disease</li></ul>

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**Bilious emesis** in a neonate is a sign of intestinal **obstruction below** the second part of the duodenum. The differential diagnosis includes midgut volvulus, which is a surgical emergency and must be excluded definitively. Other causes include **intestinal stenosis** and **atresia**. The more distal the atresia, the more likely it is to present with abdominal distension rather than bilious emesis. The absence of a segment of





**Bilious emesis** in a neonate is a sign of intestinal **obstruction below** the second part of the duodenum. The differential diagnosis includes midgut volvulus, which is a surgical emergency and must be excluded definitively. Other causes include **intestinal stenosis** and **atresia**. The more distal the atresia, the more likely it is to present with abdominal distension rather than bilious emesis. The absence of a segment of jejunum and ileum in this case confirms that the infant's condition is due to intestinal atresia.

Intestinal atresias of the midgut (eg, jejunum, ileum, proximal colon) are the result of **vascular occlusion** in utero. Diminished intestinal perfusion leads to ischemia of a segment of bowel, with subsequent narrowing (stenosis) or obliteration (atresia) of the lumen. If a major vessel (eg, the superior mesenteric artery) is occluded, the area of intestinal necrosis is large. The result is a proximal segment that ends in a blind pouch; followed by an area of absent small bowel and associated dorsal mesentery; and, finally, a distal segment of ileum that assumes a **spiral configuration** around an ileocolic vessel. This specific pattern is known as an "apple-peel" or "Christmas tree" deformity.

**(Choice A)** Improper rotation of the developing gut and the mesentery can lead to malrotation and subsequent midgut volvulus. The presentation of midgut volvulus (bilious emesis) is similar to intestinal atresia. However, the surgical findings in this case (atresia rather than malrotation) rule out midgut volvulus.







Item 7 of 40

Question Id: 319



Mark



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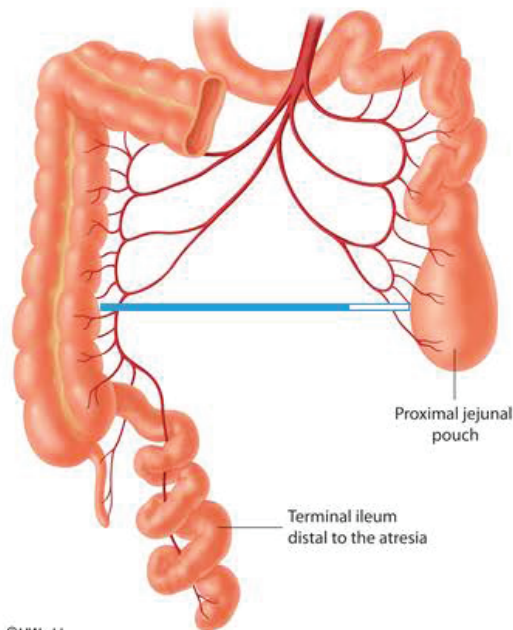
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#### Apple peel atresia



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subsequent midgut volvulus. The presentation of midgut volvulus (bilious emesis) is similar to intestinal atresia. However, the surgical findings in this case (atresia rather than malrotation) rule out midgut volvulus.

**(Choice B)** Hirschsprung disease results from the failure of neural crest cells to migrate into the distal colonic wall. Without neural crest cells, submucosal and myenteric plexi do not develop and the distal colon becomes nonfunctional. Affected infants have intestinal obstruction and failure to pass stool.

**(Choice C)** Failure of the tracheoesophageal septum to partition the foregut into the esophagus and the trachea during the 4th-5th week of gestation leads to tracheoesophageal fistula.

**(Choice D)** Duodenal atresia occurs when the duodenal lumen fails to recanalize after endothelial proliferation during the 8th-10th week of gestation. Recanalization failure is not the cause of atresia or stenosis in the distal gut; distal atresias are due to vascular injury.

### Educational objective:

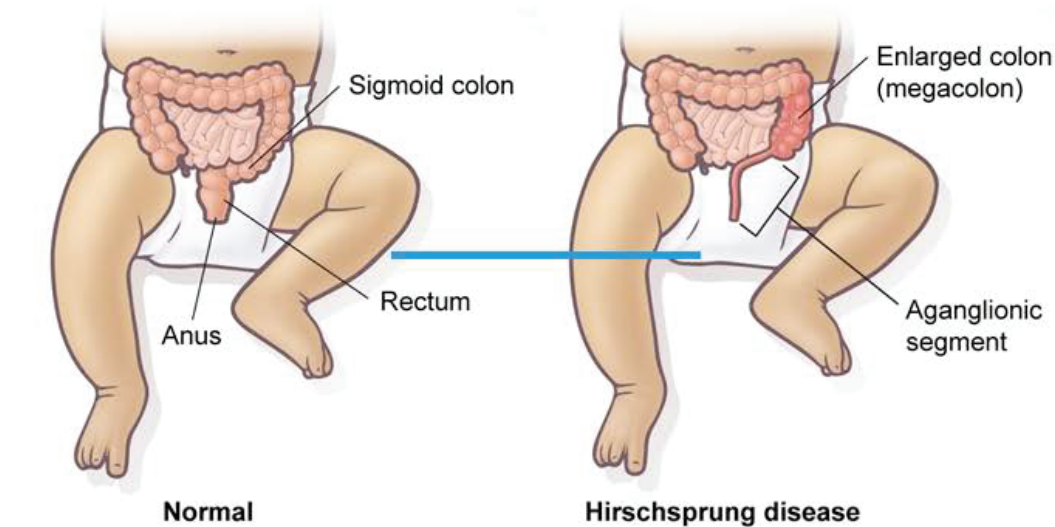
Intestinal atresia distal to the duodenum occurs due to vascular accidents in utero. "Apple-peel" atresia occurs when the superior mesenteric artery is obstructed. The result is a blind-ending proximal jejunum; a length of absent bowel and mesentery; and, finally, a terminal ileum spiraled around an ileocolic vessel.

### References



## Exhibit Display

## Hirschsprung disease



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Item 7 of 40

Question Id: 319



Mark



Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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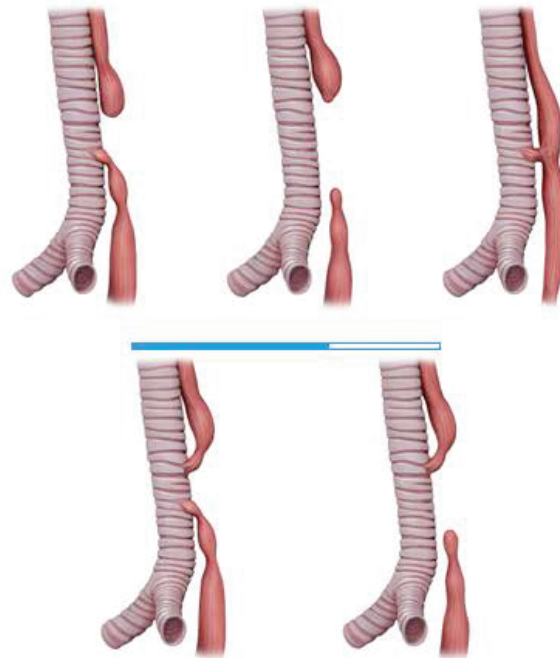


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A boy is examined in the newborn nursery shortly after birth. He was born full term by vaginal delivery to a 40-year-old woman who did not receive prenatal care. His temperature is 36.7 C (98 F), pulse is 132/min, and respirations are 38/min. Examination shows slanted palpebral fissures, epicanthal folds, thick nuchal folds, and a single palmar crease. The patient has a large, reducible midline abdominal protrusion covered by skin that is more pronounced when he cries. The umbilical stump is at the center of the protrusion. Which of the following is the most likely cause of this patient's abdominal finding?

- ☐ A. Failure of the extraembryonic gut to return to the abdominal cavity
- ☐ B. Incomplete closure of the umbilical ring
- ☐ C. Incomplete recanalization of the fetal intestinal tract
- ☐ D. Incomplete rotation of the midgut in utero
- ☐ E. Persistent processus vaginalis

**Submit**



A boy is examined in the newborn nursery shortly after birth. He was born full term by vaginal delivery to a 40-year-old woman who did not receive prenatal care. His temperature is 36.7 C (98 F), pulse is 132/min, and respirations are 38/min. Examination shows **slanted** palpebral **fissures**, **epicanthal** folds, thick nuchal folds, and a single palmar **crease**. The patient has a large, reducible midline abdominal protrusion covered by skin that is more pronounced when he cries. The umbilical stump is at the center of the protrusion. Which of the following is the most likely cause of this patient's abdominal finding?

- ☐ A. Failure of the extraembryonic gut to return to the abdominal cavity (35%)
- ☒ B. Incomplete closure of the umbilical ring (44%)
- ☐ C. Incomplete recanalization of the fetal intestinal tract (10%)
- ☐ D. Incomplete rotation of the midgut in utero (6%)
- ☐ E. Persistent processus vaginalis (3%)

Correct

44%  
Answered correctly

01 min, 39 secs  
Time Spent

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### Congenital umbilical hernia

<b>Pathophysiology</b>	<ul style="list-style-type: none"><li>• Incomplete closure of abdominal muscles</li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• Soft, nontender bulge at umbilicus</li><li>• Protrudes with increased abdominal pressure</li><li>• Typically reducible</li></ul>
<b>Management</b>	<ul style="list-style-type: none"><li>• Observe for spontaneous closure</li><li>• Elective surgery around age 5</li></ul>

This patient's examination is consistent with [Down syndrome](#) and an [umbilical hernia](#). Normally, the umbilical ring, or the congenital fascial opening for the umbilical cord, closes and forms the linea alba, a midline band of fibrous tissue. **Umbilical hernias** are caused by an **incomplete closure of the umbilical ring**, thereby allowing protrusion of bowel through the abdominal musculature. Most umbilical hernias are **reducible, asymptomatic, and resolve spontaneously** in the first few years of life.

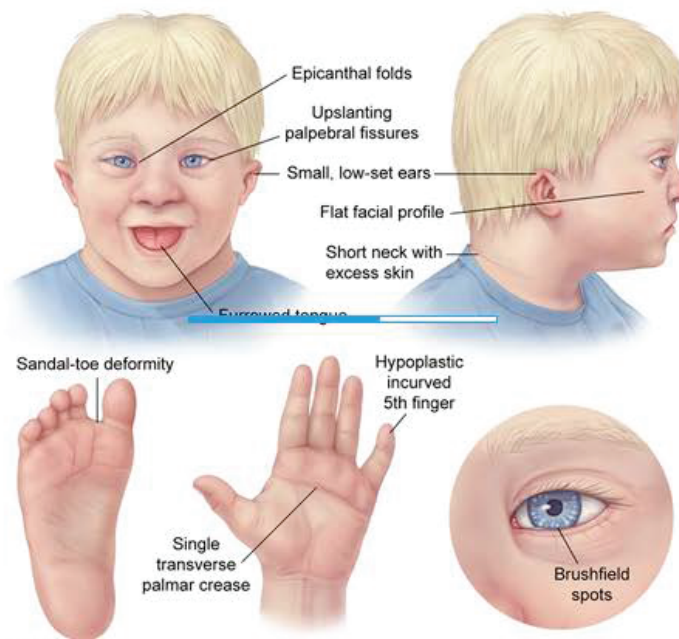
**(Choice A)** During midgut development in the first trimester, the abdominal contents undergo physiologic herniation, followed by a rotation of the midgut and physiologic reduction. Failure of this reduction can result in [omphalocele](#) or [gastroschisis](#). Omphalocele presents as a midline herniation of abdominal





## Exhibit Display

## Features of Down syndrome



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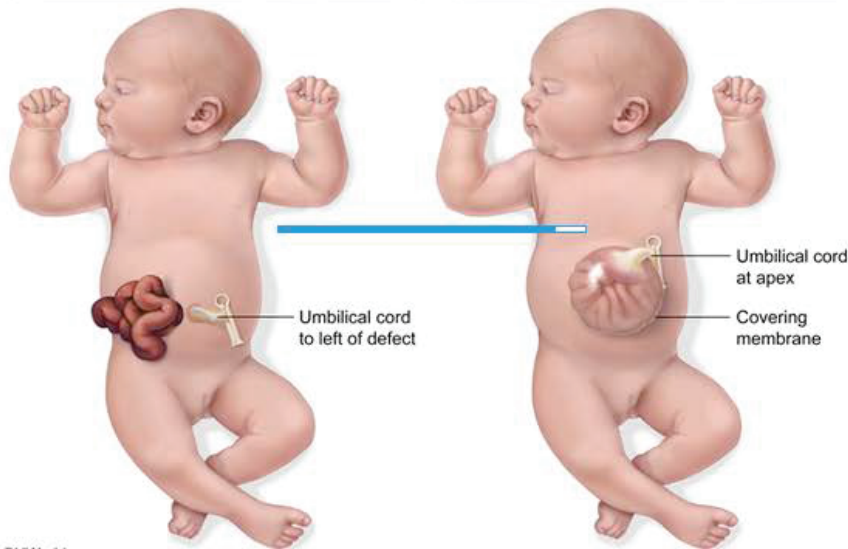
## Gastroschisis vs. omphalocele

## Gastroschisis

Eviscerated bowel with no covering membrane

## Omphalocele

Sac containing multiple organs



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result in **omphalocele** or **gastroschisis**. Omphalocele presents as a midline herniation of abdominal contents contained within a thin, membranous sac. Gastroschisis is a full-thickness abdominal wall defect that presents as an evisceration of exposed abdominal contents at birth.

**(Choice C)** Midgut development in the first trimester involves a physiologic occlusion of the intestinal lumen followed by recanalization. Failure of recanalization results in duodenal atresia, which presents with vomiting, often bilious, in the first 24 hours of life. Duodenal atresia is associated with Down syndrome.

**(Choice D)** Malrotation results from an incomplete rotation of the midgut prior to physiologic reduction into the abdominal cavity. Malrotation alone is asymptomatic. Its main complication is ischemia and subsequent small bowel necrosis due to volvulus, which twists and constricts the blood supply. Volvulus typically presents with bilious emesis in the first month of life.

**(Choice E)** Congenital inguinal hernias are formed when the processus vaginalis, an outpouching of the peritoneum, fails to obliterate, leaving a path to allow bowel contents into the inguinal canal. The hernias present as a mass in the groin and are more common in preterm male infants. Like umbilical hernias, congenital inguinal hernias are more prominent with increased abdominal pressure.

### Educational objective:

Umbilical hernias are caused by a defect in the linea alba and present as protrusions at the umbilicus that





**(Choice D)** Malrotation results from an incomplete rotation of the midgut prior to physiologic reduction into the abdominal cavity. Malrotation alone is asymptomatic. Its main complication is ischemia and subsequent small bowel necrosis due to volvulus, which twists and constricts the blood supply. Volvulus typically presents with bilious emesis in the first month of life.

**(Choice E)** Congenital inguinal hernias are formed when the processus vaginalis, an outpouching of the peritoneum, fails to obliterate, leaving a path to allow bowel contents into the inguinal canal. The hernias present as a mass in the groin and are more common in preterm male infants. Like umbilical hernias, congenital inguinal hernias are more prominent with increased abdominal pressure.

### Educational objective:

Umbilical hernias are caused by a defect in the linea alba and present as protrusions at the umbilicus that are soft, reducible, and benign. They can occur in isolation or in association with other conditions, such as Down syndrome.

### References

- [Fetal abdominal wall defects.](#)
- [Congenital and acquired umbilical hernias: examination and treatment.](#)





A 28-year-old woman at 32 weeks gestation is seen in the office for a routine prenatal visit. The patient has had burning, squeezing pain in the middle of her chest that lasts for minutes to hours at a time and usually occurs after meals. The pain is occasionally accompanied by small amounts of sour-tasting material in the back of her throat. The patient does not have any abdominal pain, emesis, or visible blood in the stool. Her pregnancy has been complicated by gestational diabetes mellitus, which has been well controlled with nutritional therapy and exercise. She does not use alcohol, tobacco, or illicit drugs. Vital signs are normal. Fundal height is 32 cm and fetal heart tones are normal. Which of the following is the most likely cause of the patient's symptoms?

- ☐ A. Decreased lower esophageal sphincter tone
- ☐ B. Delayed gastric emptying
- ☐ C. Diffuse spasm of the esophageal smooth muscle
- ☐ D. *Helicobacter pylori* infection
- ☐ E. Increased gastric acid production







had burning, squeezing pain in the middle of her chest that lasts for minutes to hours at a time and usually occurs after meals. The pain is occasionally accompanied by small amounts of sour-tasting material in the back of her throat. The patient does not have any abdominal pain, emesis, or visible blood in the stool. Her pregnancy has been complicated by gestational diabetes mellitus, which has been well controlled with nutritional therapy and exercise. She does not use alcohol, tobacco, or illicit drugs. Vital signs are normal. Fundal height is 32 cm and fetal heart tones are normal. Which of the following is the most likely cause of the patient's symptoms?

- ✓ ☒ A. Decreased lower esophageal sphincter tone (71%)
- ☐ B. Delayed gastric emptying (18%)
- ☐ C. Diffuse spasm of the esophageal smooth muscle (3%)
- ☐ D. *Helicobacter pylori* infection (1%)
- ☐ E. Increased gastric acid production (4%)

Correct

71%



49 secs



01/20/2021

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**Gastroesophageal reflux** is characterized by the retrograde movement of acidic stomach contents through the lower esophageal sphincter (LES) into the esophagus. Manifestations are most common in the minutes or hours after eating and typically include burning, squeezing pain in the retrosternal area, and the regurgitation of acidic (sour-tasting) stomach contents into the mouth.

Reflux occurs in most **pregnant women** and is common in all trimesters. The major underlying cause is **elevated estrogen and progesterone levels**, which relax the smooth muscle of the LES leading to **decreased LES tone** and reduced sensitivity to contractile stimuli (eg, high-protein meal). Later in pregnancy, reflux can also occur when the gravid uterus compresses the stomach and results in an altered LES angle or increased gastric pressure.

**(Choice B)** Delayed gastric emptying is common in those with poorly controlled diabetes mellitus due to autonomic neuropathy. It usually presents with nausea, vomiting, early satiety, and a sensation of postprandial fullness. Patients who have short periods of diabetes mellitus (eg, gestational diabetes) are unlikely to develop the autonomic damage that leads to delayed gastric emptying.

**(Choice C)** Diffuse esophageal spasm presents with difficulty swallowing solids and liquids and a sensation of food getting "stuck" in the esophagus. Pregnancy does not increase the risk of esophageal spasm.





spasm.

**(Choice D)** *Helicobacter pylori* infection can cause gastritis and peptic ulcer disease, which typically present with epigastric or abdominal pain 2–5 hours after eating (when acid is in the stomach with no food buffer). *H pylori* is not considered a predominant cause of reflux.

**(Choice E)** Increased gastric acid production is seen in Zollinger-Ellison syndrome, which is caused by the secretion of gastrin from a pancreatic or duodenal neuroendocrine tumor. Patients usually have abdominal pain (from peptic ulcers) and diarrhea. Gastric acid levels are not increased in pregnancy.

### Educational objective:

Pregnant women often develop gastroesophageal reflux disease (GERD) due to elevated levels of estrogen and progesterone, which relax the smooth muscle of the lower esophageal sphincter (LES). Later in pregnancy, GERD can also develop when the gravid uterus presses on the stomach and leads to an altered LES angle or increased gastric pressure.

### References

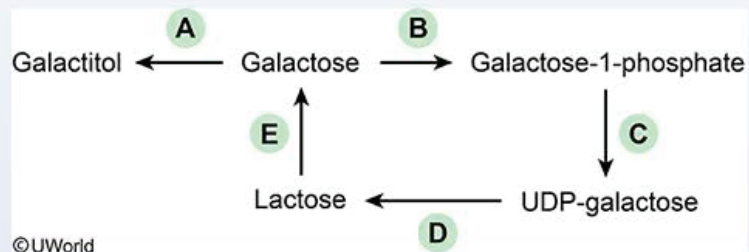
- [Review article: the management of heartburn in pregnancy.](#)
- [Gastroenterology consultations in pregnancy.](#)







A 2-year-old boy who attends daycare is brought to the emergency department due to diarrhea, fatigue, and abdominal cramps. The parents also state that he has foul-smelling, frothy stools. The boy is admitted for rehydration and subsequently diagnosed with giardiasis, which is treated with metronidazole. He improves and is discharged home. One week after discharge, the boy is seen by the primary health care provider for recurrent symptoms of frothy, loose stools and abdominal bloating and cramping. Which of the following steps of this pathway is most likely impaired in this patient?

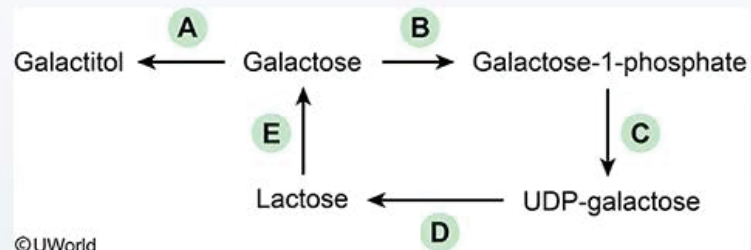


- ☐ A.A
- ☐ B.B
- ☒ C.C
- ☐ D.D





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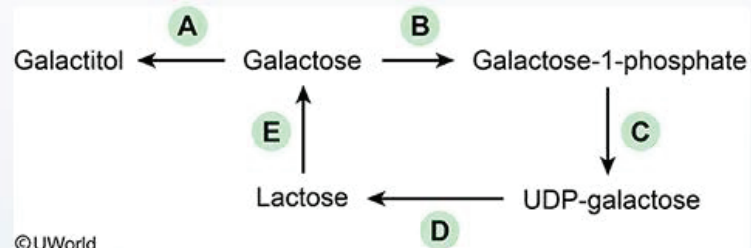


- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

**Submit**



provider for recurrent symptoms of frothy, loose stools and abdominal bloating and cramping. Which of the following steps of this pathway is most likely impaired in this patient?



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- ☐ A.A (1%)
- ☐ B.B (8%)
- ☐ C.C (9%)
- ☐ D.D (4%)
- ☒ E.E (75%)

Correct



75%

Answered correctly



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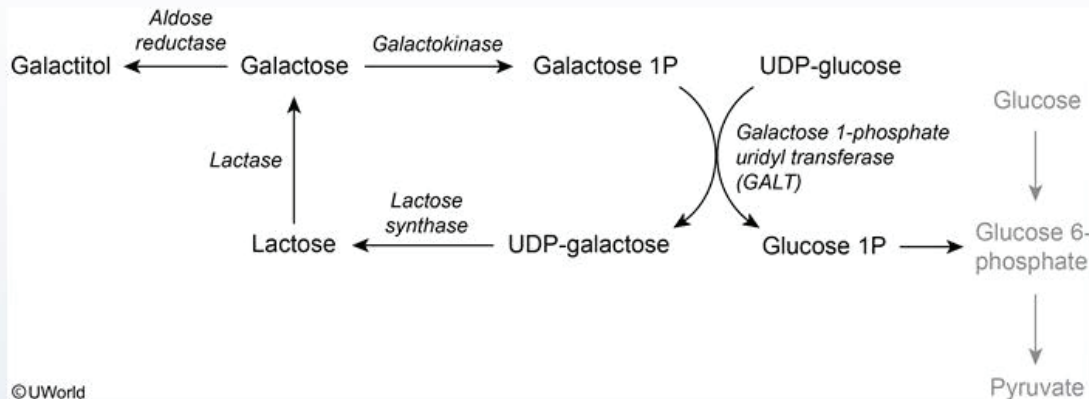


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Lactose is a disaccharide present in milk and other dairy products that is normally hydrolyzed into glucose and galactose by lactase, a brush border enzyme concentrated in epithelial cells of the small intestine.

**Lactose intolerance** is due to **decreased or absent lactase**. Malabsorbed lactose then enters the large intestine where it is fermented by bacteria, causing the clinical features of lactose intolerance: **diarrhea**, **flatulence**, and **abdominal bloating and cramping**.

Lactose intolerance can be either primary or secondary. Primary lactose intolerance is due to a genetically regulated reduction of lactase production, and its incidence increases with age. **Secondary** or acquired lactose intolerance can be due to **inflammation** (eg, celiac disease) or **infection** (eg, giardiasis) of the





lactose intolerance can be due to **inflammation** (eg, celiac disease) or **infection** (eg, giardiasis) of the small intestine, both of which cause cellular damage to the intestinal lining. The damaged cells slough off and are replaced by immature cells with low lactase concentrations, resulting in a decreased ability to convert lactose to galactose. Secondary lactose intolerance is common after giardial infections.

**(Choices A, B, and C)** Galactose-1-phosphate uridyl transferase (GALT) deficiency causes the most severe and most common form of galactosemia. Symptoms occur within the first few days of life after initiation of breastfeeding or formula and include vomiting, jaundice, hepatomegaly, and lethargy. Excess galactose is converted to galactitol by aldose reductase, resulting in cataracts from excess galactitol deposition in the lens. Galactokinase deficiency is a less common type of galactosemia, causing cataract formation only.

**(Choice D)** Lactose synthase converts UDP-galactose to lactose within the mammary glands during milk formation. Deficiency of this enzyme does not result in lactose malabsorption.

**Educational objective:**

Secondary lactase deficiency can occur after inflammatory (eg, celiac disease) or infectious (eg, giardiasis) processes damage the microvilli of the small intestines. Clinical presentation includes abdominal distension and cramping, flatulence, and diarrhea.





The mother of a 2-year-old boy calls the office for guidance regarding his recent illness. He has passed 4-6 stools daily over the last 2 days. The feces are liquid and contain no blood or mucus. His highest temperature reading at home was 37.8 C (100 F). He is eating, drinking, and being playful as usual. The patient has no prior medical problems and is up to date with vaccinations. He recently began going to day care. The mother is advised to bring the patient to the office for further evaluation. While awaiting medical evaluation, which of the following oral fluids is most effective to prevent dehydration in this patient?

- ☐ A. Chicken broth with added salt
- ☐ B. Diluted cow's milk
- ☐ C. Filtered water with no added solutes
- ☐ D. Noncarbonated sports drinks
- ☐ E. Sodium-glucose solution
- ☐ F. Sugary fruit juices

**Submit**

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- ☐ A. Chicken broth with added salt (8%)
- ☐ B. Diluted cow's milk (0%)
- ☐ C. Filtered water with no added solutes (10%)
- ☐ D. Noncarbonated sports drinks (21%)
- ☒ E. Sodium-glucose solution (58%)
- ☐ F. Sugary fruit juices (0%)





Humans consume approximately 2 L of fluid each day and secrete an additional 7 L of fluid from upper digestive organs (eg, salivary glands, stomach, pancreas, gallbladder). Nearly all of this fluid is reabsorbed from the gastrointestinal lumen by the small intestine epithelium. The **osmotic gradient** for water reabsorption is largely established by the **active cotransport of sodium** into the apical end of enterocytes coupled with chloride, glucose, or amino acids. Sodium is then transported out of the basolateral end of the enterocyte (sodium/potassium ATPase), which pulls water down its osmotic gradient from the gastrointestinal lumen through the tight junctions between enterocytes and into the lamina propria (and ultimately the bloodstream).

This young patient who recently began going to day care likely has **acute infectious diarrhea** of a viral etiology (eg, rotavirus, norovirus). Infections that target the small intestine cause watery diarrhea by blocking the active transport of sodium chloride into the enterocyte or by increasing chloride excretion into the gastrointestinal lumen (mediated by elevated intracellular cyclic AMP, cyclic GMP, or calcium). In this setting, oral rehydration with a hypotonic, **equimolar sodium-glucose solution** maximizes water and sodium reabsorption by the remaining functional enterocytes, and is the most effective oral therapy for maintaining volume and electrolyte status in children with acute infectious diarrhea.





**(Choice A)** Chicken broth with added salt is a hyperosmolar solution that can cause hyponatremia and is, therefore, not recommended.

**(Choice B)** Diluted or undiluted cow's milk is not an effective rehydration solution during acute diarrhea due to impaired digestion of milk components, which can promote osmotic diarrhea.

**(Choice C)** Filtered water alone is not usually sufficient to prevent dehydration in patients with acute infectious diarrhea due to the increased solute load in the gastrointestinal lumen, which causes most of the free water to be retained in the intestine and excreted in the feces.

**(Choices D and F)** Although sports drinks and sugary fruit juices contain glucose, they often have significantly lower sodium concentrations and high osmolality. This ultimately reduces water reabsorption and may promote osmotic diarrhea.

### Educational objective:

Children with watery diarrhea should be treated with oral rehydration solutions containing hypotonic, equimolar concentrations of sodium and glucose to help prevent dehydration and electrolyte abnormalities.

### References

- [Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy.](#)







A 65-year-old man is found to have iron deficiency anemia. He has had no cough, abdominal pain, melena, or change in bowel habits but reports anorexia and a 5-kg (11-lb) weight loss in the past 2 months. Cardiopulmonary and abdominal examinations are unremarkable. Rectal examination shows guaiac-positive brown stool. A 3-cm mass is found on colonoscopy. Biopsy shows pleomorphic cells with large, dark nuclei forming irregular, crowded glands, some of which contain mucus. Imaging studies reveal multiple mass lesions in the liver and lungs. This patient's neoplasm most likely originated from which of the following locations?

- ☐ A. Adrenal gland
- ☐ B. Ascending colon
- ☐ C. Lungs
- ☐ D. Prostate
- ☐ E. Rectosigmoid colon

**Submit**

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Feedback



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End Block



A 65-year-old man is found to have iron deficiency anemia. He has had no cough, abdominal pain, melena, or change in bowel habits but reports anorexia and a 5-kg (11-lb) weight loss in the past 2 months. Cardiopulmonary and abdominal examinations are unremarkable. Rectal examination shows guaiac-positive brown stool. A 3-cm mass is found on colonoscopy. Biopsy shows pleomorphic cells with large, dark nuclei forming irregular, crowded glands, some of which contain mucus. Imaging studies reveal multiple mass lesions in the liver and lungs. This patient's neoplasm most likely originated from which of the following locations?

- ☐ A. Adrenal gland (1%)
- ☒ B. Ascending colon (54%)
- ☐ C. Lungs (5%)
- ☐ D. Prostate (6%)
- ☐ E. Rectosigmoid colon (31%)





This elderly patient with weight loss, anorexia, and iron deficiency anemia (IDA) likely has **colon cancer**, the third most common cancer among men (after prostate and lung). It is the most common gastrointestinal malignancy and one of the most common causes of IDA in the elderly. **Right-sided colon cancers** (eg, **ascending colon**) tend to grow as large, bulky masses that protrude into the colonic lumen due to the relatively large caliber of the ascending colon. They are more likely to bleed and therefore more likely to cause IDA. The bleeding is usually occult and detected by positive fecal occult blood testing. By contrast, left-sided tumors (eg, rectosigmoid colon) tend to be smaller. They often infiltrate the wall of the colon, encircling it and narrowing the lumen. Therefore, they are more likely to cause obstruction, and patients generally have altered bowel habits, abdominal distension, and nausea and vomiting (**Choice E**). **Liver** and lung are common sites of metastases.

**(Choice A)** Malignant adrenal tumors are rare and typically present with symptoms of excessive hormone secretion (eg, Cushing syndrome). They would not cause IDA.

**(Choice C)** Although this patient has lung lesions, most patients with lung cancer have referable symptoms at presentation (eg, cough, hemoptysis, dyspnea). Hepatic metastases can occur, but a colonic mass and IDA would be unusual.







Item 12 of 40

Question Id: 257



Mark



Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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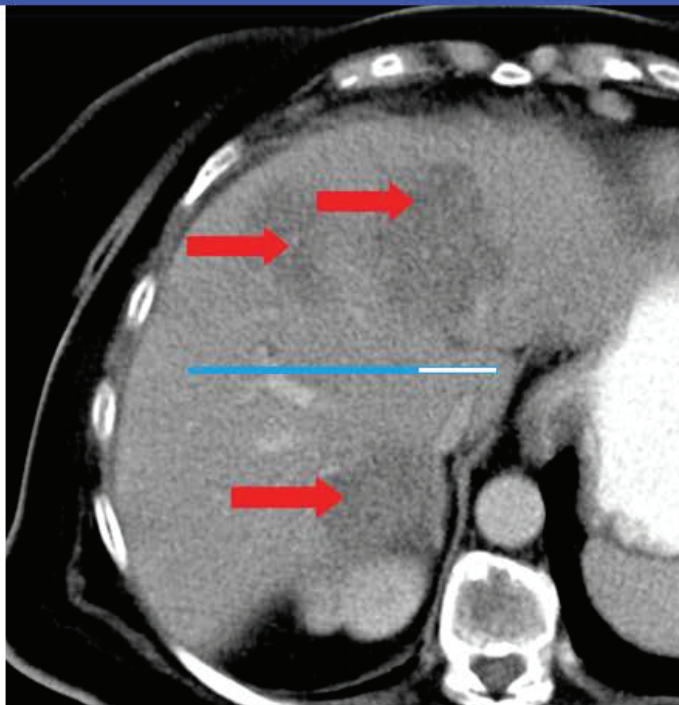


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mass and IDA would be unusual.

**(Choice D)** Prostate cancer typically develops at the gland periphery, so most patients do not have referable symptoms and urinary symptoms tend to occur late in the disease. Colonic metastases and IDA would be unusual.

### Educational objective:

Colon adenocarcinoma is the most common gastrointestinal malignancy. Right-sided lesions are more likely to bleed and cause iron deficiency anemia; left-sided lesions tend to present with obstructing symptoms (eg, altered bowel habits, constipation, abdominal distension, nausea and vomiting).

### References

- [Colorectal cancer statistics, 2014.](#)
- [Tumor location is a prognostic factor in poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma of the colon.](#)

Pathology  
Subject

Gastrointestinal & Nutrition  
System

Colorectal polyps and cancer  
Topic

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A 63-year-old man comes to the office due to intermittent rectal bleeding. The bleeding worsens with defecation and is associated with itchiness. Ten years ago, he had a kidney transplant for diabetic nephropathy and reports compliance with posttransplant immunosuppression medications. Vital signs are normal. Physical examination reveals a 2-cm ulcerated mass extending from the anal verge into the rectum. Biopsy shows large, eosinophilic squamous epithelial cells arranged in islands; cells have hyperchromatic, irregular nuclei, and scant cytoplasm. Significant keratinization is present. Which of the following factors is most likely responsible for the development of this patient's anal lesion?

- ☐ A. *BRAF* mutation
- ☒ B. Human herpesvirus 8
- ☐ C. Human papillomavirus
- ☐ D. Mismatch repair gene mutation
- ☐ E. Poxvirus
- ☐ F. *Treponema pallidum*







defecation and is associated with itchiness. Ten years ago, he had a kidney transplant for diabetic nephropathy and reports compliance with posttransplant immunosuppression medications. Vital signs are normal. Physical examination reveals a 2-cm ulcerated mass extending from the anal verge into the rectum. Biopsy shows large, eosinophilic squamous epithelial cells arranged in islands; cells have hyperchromatic, irregular nuclei, and scant cytoplasm. Significant keratinization is present. Which of the following factors is most likely responsible for the development of this patient's anal lesion?

- ☐ A. *BRAF* mutation (5%)
- ☐ B. Human herpesvirus 8 (6%)
- ☒ C. Human papillomavirus (82%)
- ☐ D. Mismatch repair gene mutation (4%)
- ☐ E. Poxvirus (0%)
- ☐ F. *Treponema pallidum* (0%)

Correct

82%  
Answered correctly01 min, 34 secs  
Time Spent11/04/2020  
Last Updated

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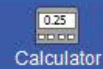
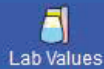
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### Anal squamous cell carcinoma

<b>Risk factors</b>	<ul style="list-style-type: none"><li>• Human papillomavirus (types 16 &amp; 18)</li><li>• Receptive anal intercourse</li><li>• Immunocompromised state (eg, HIV, organ transplant)</li><li>• Female sex</li><li>• Smoking</li></ul>
<b>Manifestations</b>	<ul style="list-style-type: none"><li>• Rectal bleeding/pain, pruritus, mass sensation</li><li>• Ulcerated or nodular anal mass</li></ul>
<b>Histology</b>	<ul style="list-style-type: none"><li>• Islands of large, eosinophilic, hyperchromatic squamous cells with scant cytoplasm &amp; nuclear atypia</li><li>• Prominent keratinization &amp;/or keratin pearls</li></ul>

This patient with a history of chronic immunosuppression has perianal bleeding and an ulcerated anal mass. In association with the classic histologic findings, this presentation suggests **anal squamous cell carcinoma** (SCC). Most patients have **rectal bleeding**, pain, or pruritus, and examination demonstrates an **ulcerated** or a nodular, exophytic anal lesion. On histology, SCCs are characterized by **large**,





### • Prominent keratinization &/or keratin pearls

This patient with a history of chronic immunosuppression has perianal bleeding and an ulcerated anal mass. In association with the classic histologic findings, this presentation suggests **anal squamous cell carcinoma** (SCC). Most patients have **rectal bleeding**, pain, or pruritus, and examination demonstrates an **ulcerated** or a nodular, exophytic anal lesion. On histology, SCCs are characterized by **large, eosinophilic, hyperchromatic squamous cells** with scant cytoplasm arranged in islands. Nuclear atypia and prominent **keratinization** and/or keratin pearls are usually observed.

Anal SCC, as well as multiple other anogenital (eg, cervical, penile, vaginal) and oropharyngeal SCCs, is strongly associated with **human papillomavirus** (HPV). HPV is a nonenveloped, double-stranded DNA virus that infects cutaneous and mucosal tissues. HPV types 16 and 18 are particularly associated with the development of malignancies. Immunocompromised states (eg, HIV, **organ transplant**) increase susceptibility to HPV infection and malignant transformation. Other risk factors include smoking, receptive anal intercourse, and female sex.

**(Choice A)** *BRAF* is a protooncogene, and mutations are associated with multiple malignancies (eg, melanoma, colon cancer, papillary thyroid cancer) but are not typically associated with anal SCC.

**(Choice B)** Human herpesvirus 8 causes Kaposi sarcoma, an angiogenic tumor that typically occurs in





melanoma, colon cancer, papillary thyroid cancer) but are not typically associated with anal SCC.

**(Choice B)** Human herpesvirus 8 causes Kaposi sarcoma, an angiogenic tumor that typically occurs in patients with severe immunosuppression (usually AIDS) but can occur in organ transplant recipients. However, it typically involves the extremities, face, or genitalia and results in painless purple or brown lesions. Histologic evaluation demonstrates whorls of spindle cells and neovascularization.

**(Choice D)** Mutations of DNA mismatch repair genes are associated with hereditary nonpolyposis colon cancer (ie, Lynch syndrome), an autosomal dominant disease that results in colonic, endometrial, and ovarian cancer. It is not associated with anal SCC.

**(Choice E)** Poxvirus causes molluscum contagiosum, which is characterized by umbilicated, flesh-colored papules with histologic findings of epidermal hyperplasia and eosinophilic, intracytoplasmic viral inclusions. Although immunocompromised patients are at increased risk of larger lesions, molluscum contagiosum is not associated with malignant transformation.

**(Choice F)** Primary syphilis (caused by *Treponema pallidum*) can result in a painless, ulcerated anogenital lesion (eg, chancre); however, bleeding is atypical, and dark-field microscopy is used to reveal the presence of spirochetes.



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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**(Choice D)** Mutations of DNA mismatch repair genes are associated with hereditary nonpolyposis colon cancer (ie, Lynch syndrome), an autosomal dominant disease that results in colonic, endometrial, and ovarian cancer. It is not associated with anal SCC.

**(Choice E)** Poxvirus causes molluscum contagiosum, which is characterized by umbilicated, flesh-colored papules with histologic findings of epidermal hyperplasia and eosinophilic, intracytoplasmic viral inclusions. Although immunocompromised patients are at increased risk of larger lesions, molluscum contagiosum is not associated with malignant transformation.

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### Educational objective:

Anal squamous cell carcinoma is strongly associated with human papillomavirus and typically presents with rectal bleeding, pruritus, and/or pain; examination demonstrates an ulcerated or nodular, exophytic anal lesion. Histology reveals large, eosinophilic, hyperchromatic squamous cells arranged in islands with nuclear atypia and prominent keratinization.

### References





A 56-year-old man comes to the cardiology clinic because of fatigue, palpitations, and exertional dyspnea over the last several weeks. On physical examination, his heart rate is irregular and measures 122 beats per minute, while his blood pressure is 110/70 mm Hg. The patient undergoes further work-up, including ECG, radiographic studies, and laboratory studies. His ECG shows atrial fibrillation and trans-esophageal echocardiography reveals a thrombus in a dilated left atrium. In the event of an interruption of blood flow secondary to arterial occlusion, which of the following organs would be least vulnerable to infarction?

- ☐ A. Spleen
- ☐ B. Brain
- ☐ C. Kidney
- ☐ D. Liver
- ☐ E. Heart

Submit







A 56-year-old man comes to the cardiology clinic because of fatigue, palpitations, and exertional dyspnea over the last several weeks. On physical examination, his heart rate is irregular and measures 122 beats per minute, while his blood pressure is 110/70 mm Hg. The patient undergoes further work-up, including ECG, radiographic studies, and laboratory studies. His ECG shows atrial fibrillation and trans-esophageal echocardiography reveals a thrombus in a dilated left atrium. In the event of an interruption of blood flow secondary to arterial occlusion, which of the following organs would be least vulnerable to infarction?

- ☐ A. Spleen (9%)
- ☐ B. Brain (7%)
- ☐ C. Kidney (4%)
- ☒ D. Liver (67%)
- ☐ E. Heart (11%)

Correct

67%  
Answered correctly

14 secs  
Time Spent

11/15/2020  
Last Updated

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Infarcts in an otherwise normal liver are rare because it has a dual blood supply: the portal vein and hepatic artery. Should the hepatic artery become occluded, the portal venous supply and retrograde arterial flow through accessory vessels (e.g., from the inferior phrenic, adrenal, intercostal arteries, etc.) is typically sufficient to sustain the liver parenchyma. The notable exception is when a transplanted liver undergoes hepatic artery thrombosis. In this case, the liver can develop biliary tree infarction and organ failure because the collateral blood supply is severed during transplantation.

**(Choice A)** The spleen is relatively vulnerable to infarction because the perfusion via the splenic artery is end-arterial. Wedge-shaped, capsule-based splenic infarcts occur and are a known complication of sickle cell anemia, infective endocarditis, and cardiac mural thrombosis.

**(Choice B)** Irreversible damage appears to occur in the most vulnerable of neurons after approximately 5 minutes of complete ischemia.

**(Choice C)** The kidney, similar to the spleen, has an end-arterial blood supply, and is generally able to tolerate warm ischemia for at least 30 minutes. Longer periods of complete ischemia result in immediate functional loss; late recovery of renal function is incomplete or absent.

**(Choice E)** The myocardium can endure complete arterial ischemia for twenty or thirty minutes without severe consequences. Briefer periods of ischemia do not result in necrosis, but rather myocardial



(Choice C) The kidney, similar to the spleen, has an end-arterial blood supply, and is generally able to tolerate warm ischemia for at least 30 minutes. Longer periods of complete ischemia result in immediate functional loss; late recovery of renal function is incomplete or absent.

(Choice E) The myocardium can endure complete arterial ischemia for twenty or thirty minutes without severe consequences. Briefer periods of ischemia do not result in necrosis, but rather myocardial stunning. Coronary artery embolism is an uncommon cause of myocardial infarction; nonetheless, it should be considered in myocardial-infarcted patients with atrial fibrillation, infective endocarditis, left atrial or ventricular thrombus, and in patients undergoing cardiac catheterization.

### Educational objective:

Organ susceptibility to infarction after occlusion of a feeding artery is ranked from greatest to least as follows: central nervous system, myocardium, kidney, spleen, and liver. The presence of a dual and/or collateral blood supply (as seen in the liver, which is supplied by the hepatic artery and portal vein) enables an organ to tolerate arterial occlusion better than those with end-arterial circulations.

### References

- [Regulation of hepatic blood flow: the hepatic arterial buffer response revisited.](#)

Anatomy    Gastrointestinal & Nutrition    Ischemic hepatitis

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An 81-year-old woman is brought to the emergency department by a neighbor due to abdominal pain. The pain comes in waves and is associated with nausea and vomiting. The patient is confused and unable to provide additional information. Past medical history is unknown, but she comes with a bag containing medications used in type 2 diabetes mellitus, hypercholesterolemia, hypertension, and dementia. On examination, the patient has a low-grade fever and mild tachycardia. She appears in distress due to pain. Mucous membranes are dry, and there is decreased skin turgor. Abdominal examination shows diffuse tenderness with high-pitched bowel sounds. Imaging of the abdomen reveals a complete small bowel obstruction. The patient undergoes laparotomy with extraction of a hard mass obstructing the ileocecal valve. The cholesterol content of the mass is 85%. Which of the following radiographic findings is most consistent with this patient's clinical presentation?

- ☐ A. Air in the biliary tree
- ☐ B. Distended bladder
- ☐ C. Free air in peritoneal cavity
- ☐ D. Heavily calcified arteries
- ☐ E. Pancreatic calcifications





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- ☐ B. Distended bladder
- ☐ C. Free air in peritoneal cavity
- ☐ D. Heavily calcified arteries
- ☐ E. Pancreatic calcifications
- ☐ F. Pleural effusion

**Submit**

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Feedback



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examination, the patient has a low-grade fever and mild tachycardia. She appears in distress due to pain.

Mucous membranes are dry, and there is decreased skin turgor. Abdominal examination shows diffuse tenderness with high-pitched bowel sounds. Imaging of the abdomen reveals a complete small bowel obstruction. The patient undergoes laparotomy with extraction of a hard mass obstructing the ileocecal valve. The cholesterol content of the mass is 85%. Which of the following radiographic findings is most consistent with this patient's clinical presentation?

- ☒ A. Air in the biliary tree (68%)
- ☐ B. Distended bladder (1%)
- ☐ C. Free air in peritoneal cavity (8%)
- ☐ D. Heavily calcified arteries (6%)
- ☐ E. Pancreatic calcifications (13%)
- ☐ F. Pleural effusion (0%)

Correct

68%  
Answered correctly

01 min, 32 secs  
Time spent

02/05/2021  
Last updated

Block Time Remaining: 00:15:00

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Item 15 of 40

Question Id: 88



Mark



Previous



Next



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Lab Values



Notes



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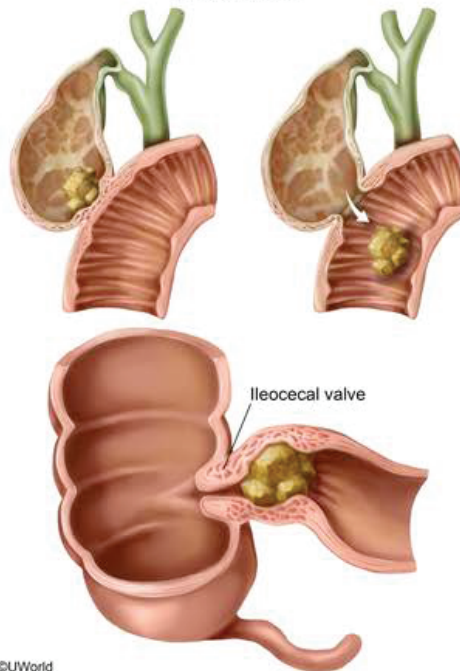
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### Exhibit Display

Gallstone ileus



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This patient, an older woman with intermittent abdominal pain and a cholesterol-containing mass lodged at the ileocecal valve, has a **gallstone ileus**. Gallstone ileus is not a true ileus (nonmechanical disruption of intestinal motility) but rather a mechanical obstruction that occurs when a large gallstone (usually >2.5 cm in diameter) erodes into the intestinal lumen through a **cholecystoenteric fistula**. As the gallstone travels down the intestine, it intermittently obstructs the lumen, causing episodic symptoms. Eventually, the gallstone may come to rest in the ileum, which has the smallest lumen of the intestinal tract.

Typical symptoms of gallstone ileus include crampy pain, vomiting, and bloating. Examination will show signs of **small bowel obstruction**, such as abdominal distension, tenderness, and high-pitched (tinkling) bowel sounds. Abdominal radiographs may reveal dilated bowel loops with air-fluid levels. Careful inspection may also reveal air in the biliary tree (**pneumobilia**) due to retrograde passage of intestinal gas through the fistula.

**(Choice B)** Bladder distension due to urinary retention is most often associated with underlying prostatic hyperplasia, anticholinergic medication use, and underlying neurologic impairment.

**(Choice C)** Air in the peritoneal cavity is suggestive of bowel perforation. Although the bowel wall is disrupted in gallstone ileus, the cholecystoenteric fistula is usually associated with fibrotic adhesions



**(Choice C)** Air in the peritoneal cavity is suggestive of bowel perforation. Although the bowel wall is disrupted in gallstone ileus, the cholecystoenteric fistula is usually associated with fibrotic adhesions between the biliary tree and the bowel, and there is no free communication with the peritoneal cavity.

**(Choice D)** Heavily calcified vessels are a sign of chronic atherosclerotic arterial disease. Common intra-abdominal complications in such patients would include intestinal ischemia and abdominal aortic aneurysm.

**(Choice E)** Pancreatic calcifications are suggestive of chronic pancreatitis, which is most commonly seen in alcohol abuse, cystic fibrosis, or outlet obstruction due to tumor, pseudocysts, or recurrent passage of gallstones.

**(Choice F)** Pleural effusion may be seen in a broad range of intra-abdominal conditions, such as pancreatitis, esophageal rupture, or chronic hepatic or renal disease.

### **Educational objective:**

Gallstone ileus is a mechanical bowel obstruction caused when a large gallstone erodes into the intestinal lumen. Pneumobilia (air in the biliary tract) is a common finding.

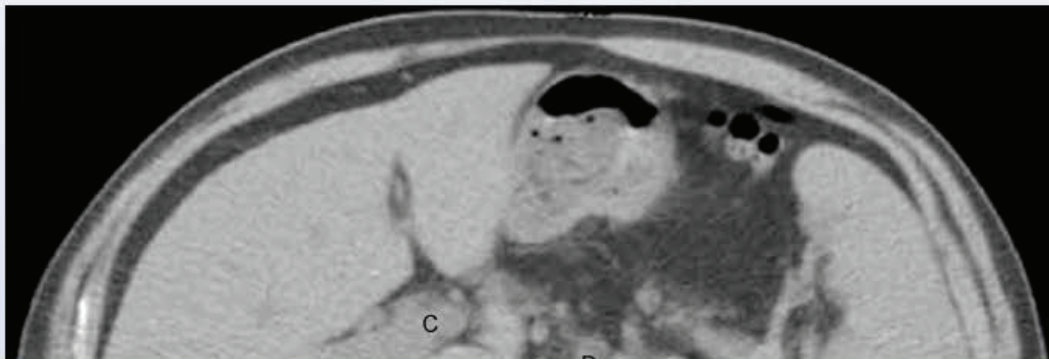
### **References**

- [Gallstone ileus: case report and literature review.](#)





A 53-year-old man who has not seen a physician in years presents to your office complaining of abdominal distention. He states "Last month my stomach started to swell up and it hasn't gotten any better". He has no other medical problems. The patient admits to drinking 10-12 beers a day for the last 20 years. His temperature is 36.7 C (98 F), blood pressure is 116/72 mm Hg, pulse is 78/min and respirations are 20/min. On examination his abdomen is distended with engorged paraumbilical veins. There is also palmar erythema and multiple spider angiomas are present. You decided to place him on a low-salt diet and start therapy with furosemide and spironolactone, with subsequent improvement of his abdominal distention. Before beginning this patient's treatment, which of the following structures labeled on the image below is expected to have an increased pressure?





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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☐ A.A

☐ B.B

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☐ A.A☒ B.B☐ C.C☐ D.D**Submit**





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Next



Full Screen



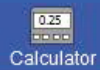
Tutorial



Lab Values



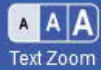
Notes



Calculator



Reverse Color



Text Zoom



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- ☐ A.A (3%)
- ☐ B.B (18%)
- ☒ C.C (71%)
- ☐ D.D (5%)

Correct

71%

33 secs

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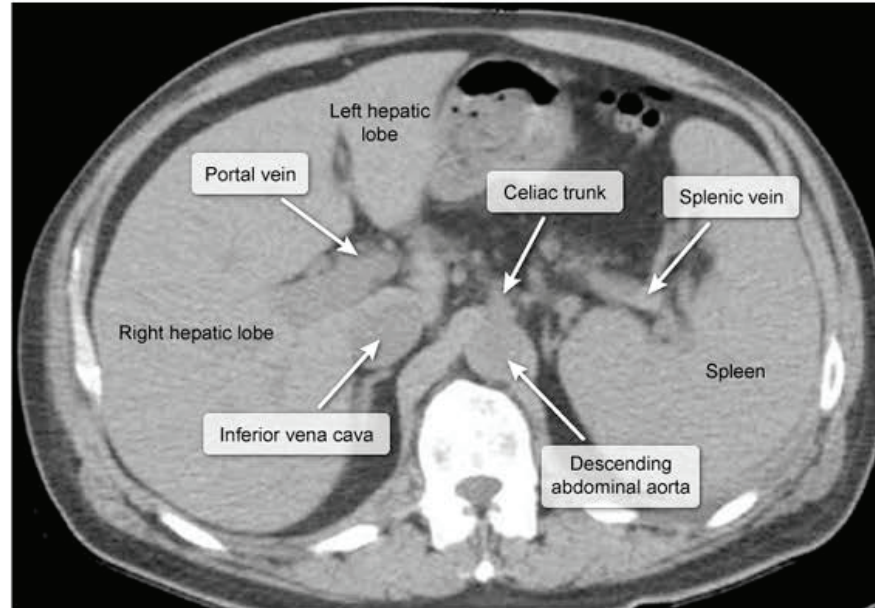
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### Exhibit Display

#### Abdominal CT anatomy



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The patient described in the question stem is likely suffering from alcoholic cirrhosis. Alcoholic cirrhosis is a form of micronodular cirrhosis associated with hepatocyte death followed by fine fibrosis of the liver. As cirrhosis worsens and the number of functioning hepatocytes decreases, the functional ability of the liver diminishes. In advanced disease, portal blood has an increasingly difficult time passing through the liver because the vasculature becomes compromised by the progressive fibrosis, causing portal hypertension. Of the structures identified on the image above, only the portal and splenic veins are part of the portal venous system. In this patient, high pressure would be expected throughout the portal system, including the superior mesenteric, portal, and splenic veins. The effects of prolonged portal hypertension include varices at the four sites of portocaval anastomoses (esophagus, rectum, umbilicus, and retroperitoneal), as well as ascites.

The pathogenesis of ascites in patients with cirrhosis is complex. In addition to mechanical compromise of portal vein flow by fibrotic tissue, vasoactive agents also play a role by causing dilatation of the splanchnic arterial vasculature and further intrahepatic vasoconstriction. These processes result in increased portal vein hydrostatic pressure leading to ascitic fluid formation, as well as decreased systemic perfusion pressure. The kidney senses the decreased perfusion pressure (accentuated by renal vasoconstriction in hepatorenal syndrome) and responds with avid retention of sodium and water, thus promoting further

Block Time Remaining: 00:15:35

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vein hydrostatic pressure leading to ascitic fluid formation, as well as decreased systemic perfusion pressure. The kidney senses the decreased perfusion pressure (accentuated by renal vasoconstriction in hepatorenal syndrome) and responds with avid retention of sodium and water, thus promoting further increase in ascitic fluid formation. Treatment of ascites secondary to cirrhosis involves restriction of sodium intake combined with diuretics. The most commonly prescribed initial therapy is a combination of furosemide and spironolactone.

**(Choice A)** The descending abdominal aorta will have elevated pressures in patients with systemic hypertension.

**(Choice B)** The inferior vena cava experiences increased pressure in cases of heart failure. This patient does not present with the typical symptoms associated with heart failure, such as lower extremity edema and shortness of breath.

**(Choice D)** The celiac trunk emerges from the aorta at this level (T12 / L1).

**Educational Objective:**

The portal vein can be identified on cross-sectional scans lying medial to (or just within) the right lobe of the liver and anterior to the inferior vena cava. The pressure in the portal system is elevated in liver cirrhosis.

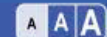




A 58-year-old man comes to the office with upper abdominal pain, fatigue, and anorexia. He says his symptoms began about a month ago and seem to be getting worse. The patient has a history of cirrhosis due to chronic hepatitis C. Physical examination shows cachexia and worsening ascites. Imaging studies reveal a large mass in the right hepatic lobe consistent with unresectable hepatocellular cancer. The patient is scheduled to undergo percutaneous embolization of the artery supplying the tumor. Contrast material administration into which of the following structures is most likely to visually enhance the artery prior to embolization?

- ☐ A. Celiac trunk
- ☐ B. Gastroduodenal artery
- ☐ C. Inferior mesenteric artery
- ☐ D. Inferior vena cava
- ☐ E. Splenic artery
- ☐ F. Superior mesenteric artery





symptoms began about a month ago and seem to be getting worse. The patient has a history of cirrhosis due to chronic hepatitis C. Physical examination shows cachexia and worsening ascites. Imaging studies reveal a large mass in the right hepatic lobe consistent with unresectable hepatocellular cancer. The patient is scheduled to undergo percutaneous embolization of the artery supplying the tumor. Contrast material administration into which of the following structures is most likely to visually enhance the artery prior to embolization?

- ☒ A. Celiac trunk (83%)
- ☐ B. Gastroduodenal artery (5%)
- ☐ C. Inferior mesenteric artery (0%)
- ☐ D. Inferior vena cava (3%)
- ☐ E. Splenic artery (1%)
- ☐ F. Superior mesenteric artery (5%)

Correct

83%



48 secs



10/19/2020

Block Time Remaining: 00:16:23

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Feedback

Suspend

End Block





Item 17 of 40

Question Id: 11760



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



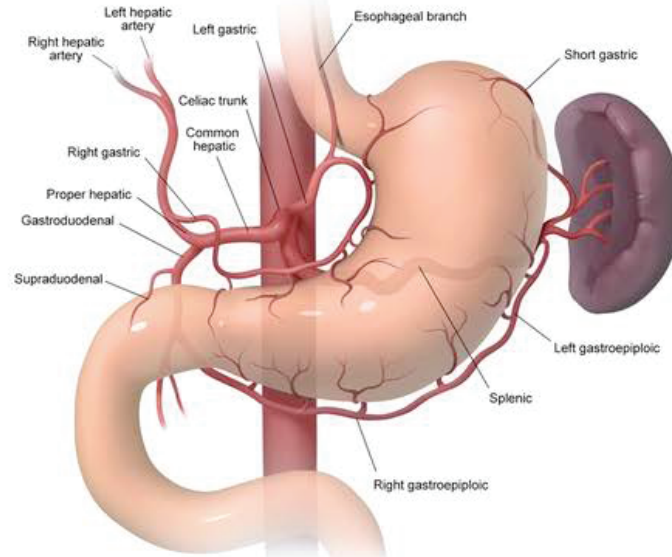
Text Zoom



Settings

## Exhibit Display

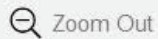
## Upper abdominal vasculature



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Block Time Remaining: 00:16:23

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Feedback



Suspend



End Block



The vascular supply to the upper abdomen mainly comes from the **celiac trunk** (celiac artery), which is the first anterior branch of the abdominal aorta. The celiac trunk branches into the left gastric, **common hepatic**, and splenic arteries. The left gastric artery further divides into the esophageal and stomach branches, which supply blood to the abdominal esophagus and upper stomach. The splenic artery and its branches (dorsal pancreatic, short gastric, left gastro-omental, and greater pancreatic arteries) provide blood to the spleen, the gastric fundus, and part of the pancreas (**Choice E**).

The common hepatic artery further divides into the gastroduodenal and proper hepatic arteries. The gastroduodenal artery supplies blood to the pylorus, proximal duodenum, and pancreatic head (**Choice B**).

The **proper hepatic** artery divides into the left and right hepatic arteries, which provide arterial blood supply to the liver and would perfuse this patient's right hepatic lobe mass.

**(Choice C)** The inferior mesenteric artery branches off the abdominal aorta at the L3 level (inferior to both the celiac trunk and superior mesenteric artery). This artery provides blood supply to the colon from the splenic flexure to the upper rectum (eg, descending and sigmoid colon).

**(Choice D)** The inferior vena cava (IVC) is formed by the union of both common iliac veins and drains blood from the lower part of the body to the right atrium. Other veins that empty into the IVC include the





the celiac trunk and superior mesenteric artery). This artery provides blood supply to the colon from the splenic flexure to the upper rectum (eg, descending and sigmoid colon).

**(Choice D)** The inferior vena cava (IVC) is formed by the union of both common iliac veins and drains blood from the lower part of the body to the right atrium. Other veins that empty into the IVC include the hepatic, renal, lumbar, and gonadal veins.

**(Choice F)** The superior mesenteric artery branches off the abdominal aorta inferior to the origin of the celiac trunk. The superior mesenteric artery supplies blood to part of the pancreas and the intestine from the lower part of the duodenum to the first two-thirds of the transverse colon.

### Educational objective:

The celiac trunk is the first main branch of the abdominal aorta; it provides oxygenated blood to the spleen, stomach, liver, abdominal esophagus, and parts of the duodenum and pancreas. The proper hepatic artery branches off the common hepatic artery from the celiac trunk and provides arterial blood supply to the liver.

Anatomy

Gastrointestinal &amp; Nutrition

Cardiovascular anatomy

Subject

System

Topic

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A 34-year-old man comes to the office due to upper abdominal pain. The patient has vague discomfort that happens mostly in the afternoon and at night and is partially relieved by food. He sometimes feels nauseated. He has had no vomiting, black or bloody stools, or weight loss. The patient takes no prescription or over-the-counter medications. Family history is negative for cancer. Upper gastrointestinal endoscopy reveals a small ulcer with a clean base in the duodenal bulb. Biopsy of which of the following sites is most likely to demonstrate the infectious agent responsible for this patient's current condition?

- ☐ A. Gastric antrum
- ☐ B. Gastric body
- ☐ C. Gastric fundus
- ☐ D. Lower duodenum
- ☐ E. Upper duodenum

Submit

Block Time Remaining: 00:16:24

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Feedback



Suspend



End Block



A 34-year-old man comes to the office due to upper abdominal pain. The patient has vague discomfort that happens mostly in the afternoon and at night and is partially relieved by food. He sometimes feels nauseated. He has had no vomiting, black or bloody stools, or weight loss. The patient takes no prescription or over-the-counter medications. Family history is negative for cancer. Upper gastrointestinal endoscopy reveals a small ulcer with a clean base in the duodenal bulb. Biopsy of which of the following sites is most likely to demonstrate the infectious agent responsible for this patient's current condition?

- ☒ A. Gastric antrum (73%)
- ☐ B. Gastric body (4%)
- ☐ C. Gastric fundus (5%)
- ☐ D. Lower duodenum (1%)
- ☐ E. Upper duodenum (14%)

Correct

73%  
Answered correctly

36 secs  
Time Spent

09/03/2020  
Last Updated

Block Time Remaining: 00:16:59

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Item 18 of 40

Question Id: 7710



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

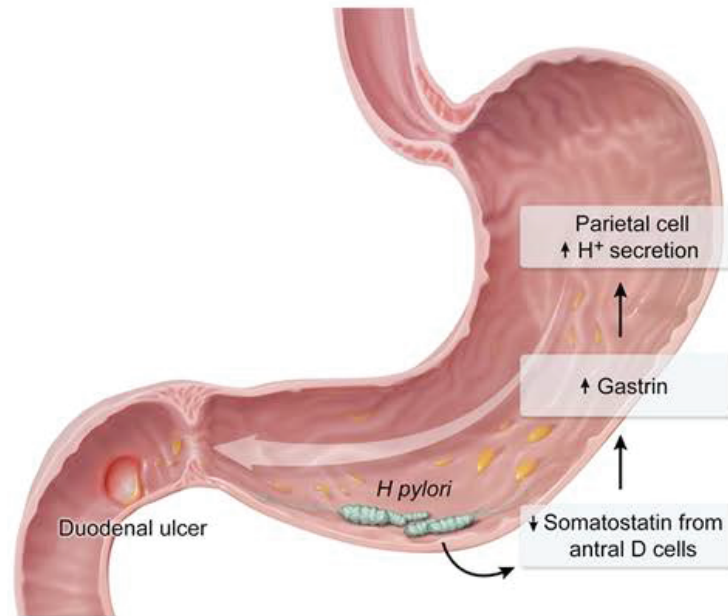
Calculator

Reverse Color

Text Zoom

Settings

## Exhibit Display

*Helicobacter pylori* and duodenal ulcers

Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:16:59

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Feedback

Suspend

End Block





Peptic (eg, duodenal, gastric, gastroesophageal) ulcers are most commonly due to ***Helicobacter pylori*** infection or use of nonsteroidal anti-inflammatory drugs. Because this patient takes no medications, his ulcer is likely due to *H pylori* infection. The site of ulcer formation is dependent on relative bacterial colonization density within the stomach. *H pylori* preferentially colonizes the gastric **antrum**, particularly early in the disease, although it may occur in other areas of the stomach or spread with time.

Colonization of *H pylori* in the **gastric antrum** is associated with **decreased somatostatin** formation and increased gastrin secretion, which stimulate the parietal cells to produce **excess acid**. This results in an increased acid load emptying into the proximal duodenum, leading to **duodenal ulcer** (DU) formation. Biopsy of the antrum can confirm *H pylori* infection in patients with a DU, which characteristically presents with upper abdominal pain that improves with eating.

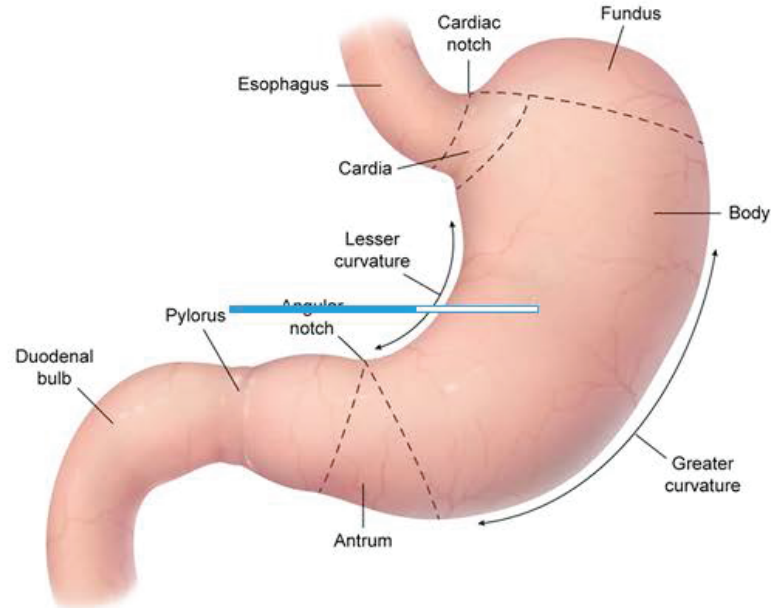
In contrast, **gastric ulcers** (GUs) are associated with colonization in the **gastric corpus** (body). The etiology of GUs is not acid related, as these patients typically have normal or reduced acid levels, but is thought to be due to **direct mucosal damage** and chronic inflammation. Unlike DU pain, GU pain often worsens with eating.

**(Choices B and C)** Patients with DUs who are infected with *H pylori* may test positive for the organism at multiple locations within the stomach. However, colonization density is highest within the antrum, not the



### Exhibit Display

#### Regions of the stomach



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Feedback

Suspend

End Block

thought to be due to **direct mucosal damage** and chronic inflammation. Unlike DU pain, GU pain often worsens with eating.

**(Choices B and C)** Patients with DUs who are infected with *H pylori* may test positive for the organism at multiple locations within the stomach. However, colonization density is highest within the antrum, not the gastric body or the gastric fundus; therefore, the antrum is the optimal site for biopsy.

**(Choices D and E)** Although the ulcer occurs in the duodenum, high concentrations of *H pylori* are not typically found in the duodenal regions, as *H pylori* can colonize only gastric tissue or areas of gastric metaplasia.

### Educational objective:

*Helicobacter pylori* is a common cause of peptic ulcers. Duodenal ulcers are associated with heavy colonization in the gastric antrum, whereas colonization in the gastric corpus is associated with gastric ulcers.

Pathology  
Subject

Gastrointestinal & Nutrition  
System

Peptic ulcer disease  
Topic

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Feedback

Suspend

End Block

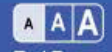




A 26-year-old previously healthy man is brought to the emergency department after a motor vehicle collision. The patient was driving while wearing a seatbelt when his car was hit on the left side by another vehicle. He has since had persistent left shoulder pain. He also has nausea and hiccups. The patient's blood pressure is 90/60 mm Hg and pulse is 115/min. On examination, he has a bruise on the left lower chest wall with tenderness to palpation along the area. Chest auscultation reveals normal heart sounds and bilaterally equal breath sounds. He has a rigid and tender abdomen. Which of the following is the most likely diagnosis?

- ☐ A. Aortic rupture
- ☐ B. Hemopericardium
- ☐ C. Humerus fracture
- ☐ D. Lung contusion
- ☐ E. Myocardial contusion
- ☐ F. Pneumothorax
- ☐ G. Splenic laceration





vehicle. He has since had persistent left shoulder pain. He also has nausea and hiccups. The patient's

blood pressure is 90/60 mm Hg and pulse is 115/min. On examination, he has a bruise on the left lower chest wall with tenderness to palpation along the area. Chest auscultation reveals normal heart sounds and bilaterally equal breath sounds. He has a rigid and tender abdomen. Which of the following is the most likely diagnosis?

- ☐ A. Aortic rupture (3%)
- ☐ B. Hemopericardium (4%)
- ☐ C. Humerus fracture (0%)
- ☐ D. Lung contusion (3%)
- ☐ E. Myocardial contusion (1%)
- ☐ F. Pneumothorax (1%)
- ☒ G. Splenic laceration (85%)

Correct



85%

Answered correctly



01 min, 02 secs

Time spent



10/23/2020

Last updated

Block Time Remaining: 00:18:01

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Feedback



Suspend



End Block



This patient's rigid abdomen with associated left shoulder pain, hypotension, and tachycardia suggests a possible **splenic laceration** and hemoperitoneum. The shoulder pain likely represents referred pain due to peritoneal irritation (**Kehr sign**).

The phrenic nerves originate from C3-C5 and pass between the lung and heart to provide motor function to the diaphragm. The phrenic nerves also provide sensory fibers to the pericardium, mediastinal pleura, and diaphragmatic peritoneum. The supraclavicular nerves originate from C3-C4 and their branches innervate the sternoclavicular joint, local muscles (eg, sternocleidomastoid), and the skin of the upper and posterior shoulder. Any abdominal process (eg, ruptured spleen, peritonitis, hemoperitoneum) irritating the sensory fibers around the diaphragm can cause **referred pain** via the phrenic nerve to the C3-C5 shoulder region. Phrenic nerve irritation can also cause **hiccups** due to spasmodic diaphragmatic contraction pulling air against a closed larynx.

**(Choice A)** Traumatic aortic rupture presents with chest wall contusions and hypotension, but it is not typically associated with persistent left shoulder pain or hiccups.

**(Choices B and D)** Hemopericardium (blood accumulation in the pericardial sac) typically presents with shortness of breath, tachycardia, jugular venous distention, and possible hypotension. Lung contusion usually presents gradually with shortness of breath, chest pain, and consolidation on lung imaging.







**(Choices B and D)** Hemopericardium (blood accumulation in the pericardial sac) typically presents with shortness of breath, tachycardia, jugular venous distention, and possible hypotension. Lung contusion usually presents gradually with shortness of breath, chest pain, and consolidation on lung imaging. However, persistent shoulder pain is not commonly associated with either condition.

**(Choice C)** Humerus fracture typically presents with acute shoulder pain that is increased with movement. Examination can show a deformed shoulder joint. This patient's rigid abdomen and absence of obvious shoulder abnormalities make this less likely.

**(Choice E)** Myocardial contusion after chest wall trauma typically presents with mid-anterior chest wall pain, shortness of breath, persistent tachycardia, and new conduction defects on ECG (eg, bundle branch block). It is not typically associated with persistent abdominal or shoulder pain.

**(Choice F)** Pneumothorax after chest trauma usually presents with tachypnea, shortness of breath, decreased or absent breath sounds, unilateral hyperresonance to percussion, and pleuritic chest pain. This patient's bilaterally equal breath sounds make this unlikely.

**Educational objective:**

Any abdominal process (eg, ruptured spleen, peritonitis, hemoperitoneum) irritating the phrenic nerve sensory fibers around the diaphragm can cause referred pain to the C3-C5 shoulder region (Kehr sign).





**(Choice C)** Humerus fracture typically presents with acute shoulder pain that is increased with movement. Examination can show a deformed shoulder joint. This patient's rigid abdomen and absence of obvious shoulder abnormalities make this less likely.

**(Choice E)** Myocardial contusion after chest wall trauma typically presents with mid-anterior chest wall pain, shortness of breath, persistent tachycardia, and new conduction defects on ECG (eg, bundle branch block). It is not typically associated with persistent abdominal or shoulder pain.

**(Choice F)** Pneumothorax after chest trauma usually presents with tachypnea, shortness of breath, decreased or absent breath sounds, unilateral hyperresonance to percussion, and pleuritic chest pain. This patient's bilaterally equal breath sounds make this unlikely.

### Educational objective:

Any abdominal process (eg, ruptured spleen, peritonitis, hemoperitoneum) irritating the phrenic nerve sensory fibers around the diaphragm can cause referred pain to the C3-C5 shoulder region (Kehr sign).

### References

- [Traditional Kehr's sign: Left shoulder pain related to splenic abscess.](#)

Anatomy

Gastrointestinal & Nutrition

Spleen rupture

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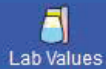
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Suspend



End Block



A 45-year-old woman comes to the office for evaluation of dysphagia. The patient's symptoms first began 2 years ago with regurgitation and bloating after meals but have recently progressed to difficulty swallowing both solid foods and liquids. She has been using antacids without relief. The patient has no other medical history. She drinks 1 or 2 beers on weekends but does not smoke or use illicit drugs. Family history is unremarkable. Vital signs are within normal limits. BMI is 21 kg/m<sup>2</sup>. The abdomen is nontender and soft with normal active bowel sounds. The patient undergoes upper endoscopy that shows a dilated esophagus and retained food. Esophageal manometry reveals increased lower esophageal sphincter (LES) tone and incomplete relaxation. Peristalsis is absent in the distal esophagus. Injection of which of the following into the patient's LES would most likely help relieve her symptoms?

- ☐ A. Botulinum toxin
- ☐ B. Corticosteroids
- ☐ C. Neostigmine
- ☐ D. Phenylephrine
- ☐ E. Pilocarpine







2 years ago with regurgitation and bloating after meals but have recently progressed to difficulty swallowing both solid foods and liquids. She has been using antacids without relief. The patient has no other medical history. She drinks 1 or 2 beers on weekends but does not smoke or use illicit drugs. Family history is unremarkable. Vital signs are within normal limits. BMI is 21 kg/m<sup>2</sup>. The abdomen is nontender and soft with normal active bowel sounds. The patient undergoes upper endoscopy that shows a dilated esophagus and retained food. Esophageal manometry reveals increased lower esophageal sphincter (LES) tone and incomplete relaxation. Peristalsis is absent in the distal esophagus. Injection of which of the following into the patient's LES would most likely help relieve her symptoms?

- ☒ A. Botulinum toxin (78%)
- ☐ B. Corticosteroids (1%)
- ☐ C. Neostigmine (9%)
- ☐ D. Phenylephrine (2%)
- ☐ E. Pilocarpine (7%)





**Achalasia** is an esophageal motility disorder characterized by the absence of esophageal peristalsis in the distal esophagus and incomplete relaxation of a **hypertonic lower esophageal sphincter** (LES).

Achalasia is caused by the immune-mediated **destruction of inhibitory ganglion cells** in the esophageal wall. Nitric oxide-producing neurons in the myenteric plexus that are responsible for esophageal smooth muscle relaxation are preferentially destroyed, whereas excitatory cholinergic neurons responsible for smooth muscle contraction are relatively spared. This imbalance results in increased lower esophageal tone and impaired sphincter relaxation.

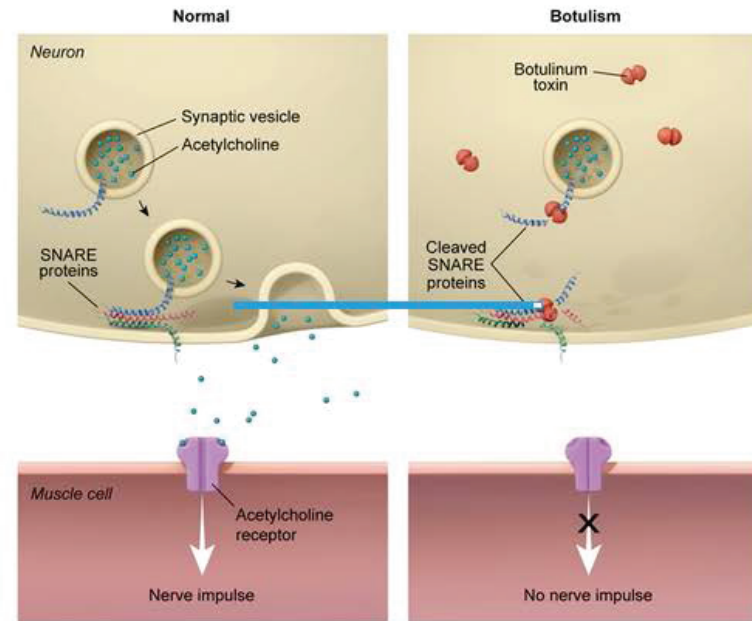
**Botulinum toxin**, a neurotoxin formed by *Clostridium botulinum*, prevents the fusion of acetylcholine-containing synaptic vesicles with the plasma membrane. This effectively prevents acetylcholine release into the neuromuscular synapse, resulting in muscle weakness and paralysis. In a patient with achalasia, injection of **botulinum toxin** into the LES causes **cholinergic blockade**, leading to sphincter relaxation and symptomatic improvement.

**(Choices B and D)** In addition to the cholinergic neurons, there are multiple other hormones and neurotransmitters that modulate esophageal tone. Prostaglandins promote LES relaxation, whereas alpha-adrenergic agonists, such as phenylephrine, increase LES tone. Because corticosteroids inhibit prostaglandin synthesis, both corticosteroids and phenylephrine would worsen the patient's symptoms.



## Exhibit Display

## Botulism



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prostaglandin synthesis both corticosteroids and phenylephrine would worsen the patient's symptoms

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and symptomatic improvement.

**(Choices B and D)** In addition to the cholinergic neurons, there are multiple other hormones and neurotransmitters that modulate esophageal tone. Prostaglandins promote LES relaxation, whereas alpha-adrenergic agonists, such as phenylephrine, increase LES tone. Because corticosteroids inhibit prostaglandin synthesis, both corticosteroids and phenylephrine would worsen the patient's symptoms.

**(Choices C and E)** Neostigmine is a cholinesterase inhibitor and pilocarpine is a cholinergic agonist. Both of these medications increase cholinergic stimuli at the LES and would worsen the patient's symptoms.

### Educational objective:

Achalasia is caused by loss of inhibitory ganglion cells in the distal esophageal wall and is characterized by the absence of esophageal peristalsis and incomplete relaxation of a hypertonic lower esophageal sphincter. Botulinum toxin prevents acetylcholine release into the neuromuscular synapse, resulting in inhibition of cholinergic neurons and lower esophageal sphincter relaxation.

Pharmacology

Gastrointestinal & Nutrition

Achalasia

Subject

System

Topic

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Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

A 52-year-old woman is evaluated for a 6-month history of progressive fatigue and generalized pruritus. She has had no significant prior medical conditions or surgery and takes no medications. The patient does not use tobacco, alcohol, or illicit drugs. Her sister has Sjögren syndrome. Physical examination shows skin excoriations and mild hepatomegaly. Laboratory results are as follows.

Alkaline phosphatase 480 U/L

Aspartate aminotransferase (SGOT) 37 U/L

Alanine aminotransferase (SGPT) 49 U/L

Antimitochondrial antibody positive

The pathogenesis of this patient's disease process most closely resembles that of which of the following conditions?

- ☐ A. Acetaminophen toxicity
- ☐ B. Alcoholic hepatitis
- ☐ C. Budd-Chiari syndrome



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Aspartate aminotransferase (SGOT) 37 U/L

Alanine aminotransferase (SGPT) 49 U/L

Antimitochondrial antibody positive

The pathogenesis of this patient's disease process most closely resembles that of which of the following conditions?

- ☐ A. Acetaminophen toxicity
- ☐ B. Alcoholic hepatitis
- ☐ C. Budd-Chiari syndrome
- ☐ D. Graft versus host disease
- ☒ E. Hemochromatosis
- ☐ F. Reye syndrome

Submit

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Feedback

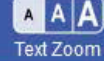
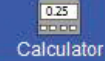
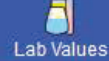
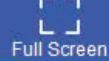


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End Block





Aspartate aminotransferase (SGOT) 37 U/L

Alanine aminotransferase (SGPT) 49 U/L

Antimitochondrial antibody positive

The pathogenesis of this patient's disease process most closely resembles that of which of the following conditions?

- ☐ A. Acetaminophen toxicity (2%)
- ☐ B. Alcoholic hepatitis (6%)
- ☐ C. Budd-Chiari syndrome (14%)
- ☒ D. Graft versus host disease (59%)
- ☐ E. Hemochromatosis (9%)
- ☐ F. ~~Reye syndrome~~ (7%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



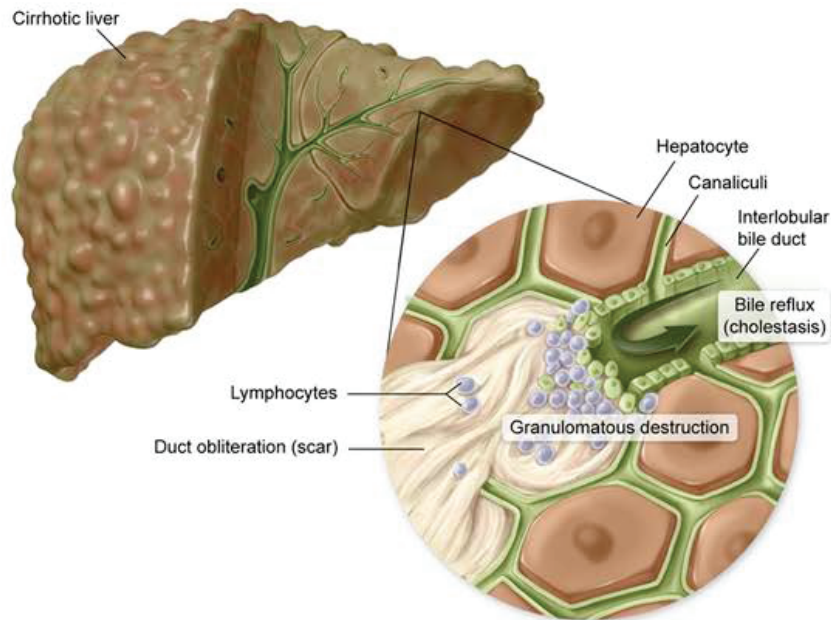
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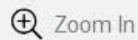
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## Exhibit Display

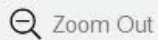
## Primary biliary cholangitis



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New



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1



Feedback



Suspend



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Previous



Next



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Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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**Primary biliary cholangitis** (PBC, formerly primary biliary cirrhosis) is a chronic **autoimmune liver disease** characterized by destruction of small and mid-sized intrahepatic bile ducts with resulting cholestasis. It is most common in middle-aged women and is frequently associated with other autoimmune disorders (eg, Sjögren syndrome, rheumatoid arthritis). Clinical features include fatigue, itching, and hepatomegaly. Serum alkaline phosphatase is elevated, and **antimitochondrial antibody** titers are positive in most cases. Biopsy findings in PBC typically show patchy **lymphocytic inflammation**, leading to granulomatous **destruction of intrahepatic bile ducts** (ie, florid duct lesion), with necrosis and micronodular regeneration of periportal tissues.

Of the diseases listed, only **graft versus host disease** (GVHD) causes similar **immune-mediated** destruction of intrahepatic bile ducts. GVHD occurs in immunocompromised patients following transplant of allogeneic bone marrow or other lymphocyte-rich tissues (eg, nonirradiated blood). Donor T-cells migrate into host tissues, where they recognize host major histocompatibility complex antigens as foreign. Liver involvement is often heralded by a rise in alkaline phosphatase and characterized histologically by **lymphocytic infiltration** and **destruction of small intrahepatic bile ducts**, highlighting the **immunologic etiology** of both diseases.

**(Choice A)** Serious acetaminophen overdose causes direct hepatocellular toxicity resulting in liver failure.

Block Time Remaining: 00:19:18

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1



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**lymphocytic infiltration and destruction of small intrahepatic bile ducts**, highlighting the **immunologic etiology** of both diseases.

**(Choice A)** Serious acetaminophen overdose causes direct hepatocellular toxicity resulting in liver failure with centrilobular necrosis that can extend to include entire lobules.

**(Choice B)** Alcoholic hepatitis (due to toxicity from chronic ethanol ingestion) is characterized by hepatocellular swelling and necrosis, steatosis, **Mallory bodies**, neutrophilic infiltration, and fibrosis.

**(Choice C)** Budd-Chiari syndrome is due to occlusion of the hepatic veins with a resulting increase in intrahepatic pressure. Gross findings include hepatomegaly with a tense capsule and reddish-purple parenchyma. Typical microscopic findings include severe centrilobular congestion and necrosis.

**(Choice E)** Hemochromatosis is due to abnormal iron absorption and results in deposition of hemosiderin in the liver. Biopsy is characterized by **visible iron** within hepatocytes.

**(Choice F)** Reye syndrome occurs in children with underlying inborn errors in metabolism; acute viral illness (often with concomitant aspirin use) promotes mitochondrial injury and subsequent alterations in metabolism that result in encephalopathy and hepatic dysfunction. Biopsy demonstrates panlobular microvesicular steatosis.

**Educational objective:**

Block Time Remaining: 00:19:18

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1



Feedback



Suspend

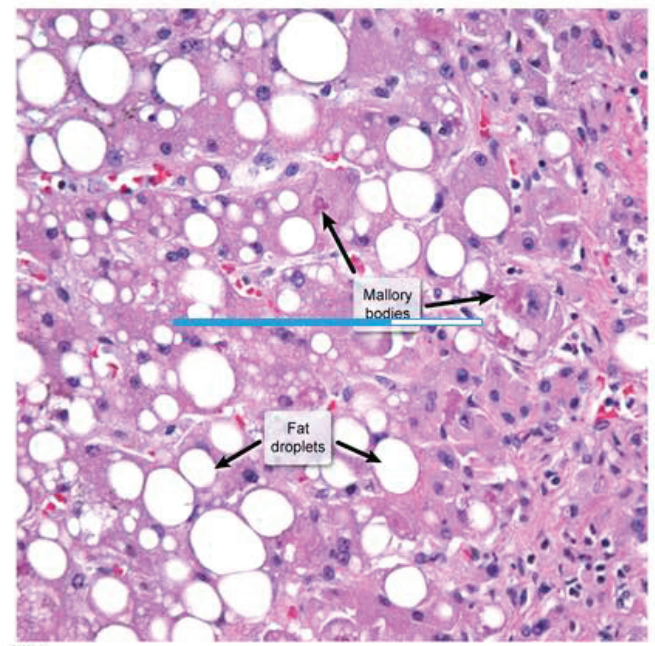


End Block

lymphocytic infiltration and destruction of small intrahepatic bile ducts highlighting the immunologic

Exhibit Display

Alcoholic liver disease



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Zoom In

Zoom Out

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Educational objective:

Block Time Remaining: 00:19:18

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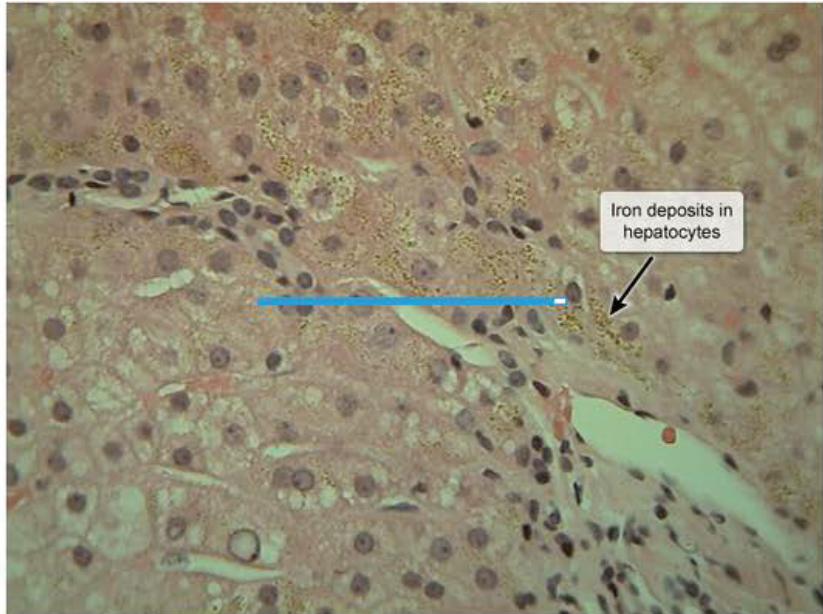
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End Block

lymphocytic infiltration and destruction of small intrahepatic bile ducts highlighting the immunologic

Exhibit Display

Hereditary hemochromatosis



Iron deposits in hepatocytes

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Educational objective:

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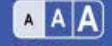


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Suspend

End Block





intrahepatic pressure. Gross findings include hepatomegaly with a tense capsule and reddish-purple parenchyma. Typical microscopic findings include severe centrilobular congestion and necrosis.

**(Choice E)** Hemochromatosis is due to abnormal iron absorption and results in deposition of hemosiderin in the liver. Biopsy is characterized by **visible iron** within hepatocytes.

**(Choice F)** Reye syndrome occurs in children with underlying inborn errors in metabolism; acute viral illness (often with concomitant aspirin use) promotes mitochondrial injury and subsequent alterations in metabolism that result in encephalopathy and hepatic dysfunction. Biopsy demonstrates panlobular microvesicular steatosis.

### Educational objective:

Primary biliary cholangitis is a chronic autoimmune liver disease characterized by lymphocytic infiltrates and destruction of small and mid-sized intrahepatic bile ducts. Similar findings are seen in hepatic graft versus host disease, highlighting the immunologic etiology of both disorders.

### References

- [Aspects of the pathophysiology of primary biliary cirrhosis.](#)

Pathophysiology

Subject

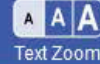
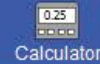
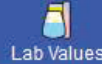
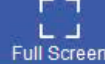
Gastrointestinal &amp; Nutrition

System

Primary biliary cholangitis

Topic





A 54-year-old man comes to the emergency department after vomiting blood. He has also had melena, fatigue, and lethargy over the last 24 hours. The patient emigrated from sub-Saharan Africa 20 years ago and occasionally returns to visit friends and family. Temperature is 37.5 C (99.5 F), blood pressure is 90/60 mm Hg, and pulse is 115/min. Abdominal palpation reveals an enlarged liver and a spleen tip below the level of the umbilicus. Laboratory results are as follows:

#### Complete blood count

Hemoglobin	5.2 g/dL
Platelets	75,000/mm <sup>3</sup>
Leukocytes	8,000/mm <sup>3</sup>
Neutrophils	79%
Eosinophils	15%
Lymphocytes	6%

Upper endoscopy reveals bleeding esophageal varices. Which of the following is the most likely underlying cause of this patient's symptoms?





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Leukocytes 8,000/mm<sup>3</sup>

Neutrophils 79%

Eosinophils 15%

Lymphocytes 6%

Upper endoscopy reveals bleeding esophageal varices. Which of the following is the most likely underlying cause of this patient's symptoms?

- ☐ A. Cysticercosis
- ☐ B. Hookworm infection
- ☐ C. Malaria
- ☐ D. Schistosomiasis
- ☐ E. Toxoplasmosis

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1



Feedback



Suspend



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Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Leukocytes

8,000/mm<sup>3</sup>

Neutrophils

79%

Eosinophils

15%

Lymphocytes

6%

Upper endoscopy reveals bleeding esophageal varices. Which of the following is the most likely underlying cause of this patient's symptoms?

- ☐ A. Cysticercosis (5%)
- ☐ B. Hookworm infection (12%)
- ☐ C. Malaria (18%)
- ☒ D. Schistosomiasis (62%)
- ☐ E. Toxoplasmosis (0%)

Correct

62%



16 secs



02/01/2021

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## Schistosomiasis

<b>Schistosoma species</b>	<b>Location</b>	<b>Symptoms</b>
<i>S haematobium</i>	<ul style="list-style-type: none"><li>• North Africa</li><li>• Sub-Saharan Africa</li><li>• Middle East</li></ul>	<b>Urinary schistosomiasis</b> <ul style="list-style-type: none"><li>• Terminal hematuria, dysuria &amp; frequent urination</li><li>• Hydronephrosis, pyelonephritis &amp; squamous cell carcinoma of the bladder</li></ul>
<i>S mansoni</i>	<ul style="list-style-type: none"><li>• Sub-Saharan Africa</li><li>• Middle East</li><li>• South America</li><li>• Caribbean</li></ul>	<b>Intestinal schistosomiasis</b> <ul style="list-style-type: none"><li>• Diarrhea &amp; abdominal pain</li><li>• Intestinal ulceration → iron deficiency anemia</li></ul>
<i>S japonicum</i>	<ul style="list-style-type: none"><li>• Asia, particularly China</li><li>• Philippines</li></ul>	<b>Hepatic schistosomiasis</b> <ul style="list-style-type: none"><li>• Hepatomegaly, splenomegaly</li><li>• Periportal fibrosis &amp; subsequent portal hypertension</li></ul>

*S japonicum*

- Asia, particularly China
- Philippines
- Japan

- Hepatomegaly, splenomegaly
- Periportal fibrosis & subsequent portal hypertension

Esophageal varices and splenomegaly are signs of **portal hypertension**, which usually indicates underlying hepatic fibrosis. Although chronic viral hepatitis and alcohol abuse are the leading causes of hepatic fibrosis in the United States, this patient's immigration/travel history and eosinophilia raise suspicion for **hepatosplenic schistosomiasis**, a parasitic blood fluke infection seen primarily in rural parts of **sub-Saharan Africa** and East Asia.

Exposure to *Schistosoma* occurs when humans swim in freshwater contaminated by infected snails (the intermediate host). Cercariae penetrate human skin and migrate to the liver, where they mature to adult worms. Adult worms then spread through the **portal circulation** to the mesenteric venules or venous plexus of the bladder. Here, they release eggs into host tissue that are excreted in the feces or urine.

Although many patients with schistosomiasis are asymptomatic, chronic exposure to *Schistosoma* eggs can activate hepatic stellate cells, leading to collagen deposition in periportal spaces and progressive **periportal fibrosis**. Occlusion of periportal veins eventually blocks venous outflow from abdominal





**periportal fibrosis.** Occlusion of periportal veins eventually blocks venous outflow from abdominal

organs, leading to **congestive splenomegaly** and **gastroesophageal varices**. Patients frequently have anemia from intestinal/variceal bleeding, thrombocytopenia from splenic trapping of platelets, and **eosinophilia** in response to adult worms.

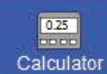
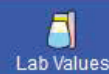
**(Choice A)** Cysticercosis is caused by ingestion of *Taenia solium* eggs from contaminated pork. Although initial infections are usually asymptomatic, patients may develop seizures years or decades later due to calcified granulomas at the site of previous brain infection. Muscle and subcutaneous tissue can also be involved, but the liver and hepatic venous system is generally not affected.

**(Choice B)** Hookworm infection is a common cause of chronic, iron-deficiency anemia and eosinophilia, but this organism does not invade the liver or portal venous system; therefore, gastric varices and hepatosplenomegaly would be atypical.

**(Choice C)** Malaria is common in patients who return to endemic areas (eg, sub-Saharan Africa) after being away (due to waning partial immunity). Although hepatosplenomegaly and anemia are common, most patients are acutely ill (eg, fever, chills, malaise), and portal hypertension and eosinophilia are generally not present.

**(Choice E)** Toxoplasmosis is most common in patients with AIDS. It usually presents with meningoencephalitis (eg, confusion, headache, vomiting). Upper gastrointestinal bleeding from





hepatosplenomegaly would be atypical.

**(Choice C)** Malaria is common in patients who return to endemic areas (eg, sub-Saharan Africa) after being away (due to waning partial immunity). Although hepatosplenomegaly and anemia are common, most patients are acutely ill (eg, fever, chills, malaise), and portal hypertension and eosinophilia are generally not present.

**(Choice E)** Toxoplasmosis is most common in patients with AIDS. It usually presents with meningoencephalitis (eg, confusion, headache, vomiting). Upper gastrointestinal bleeding from esophageal varices and eosinophilia would be atypical.

### Educational objective:

Schistosomiasis, a parasitic blood fluke infection, is common in rural portions of sub-Saharan Africa. Initial infection is often asymptomatic, but some patients develop chronic hepatosplenic (eg, portal hypertension, hepatosplenomegaly, esophageal varices) or urinary (eg, bladder cancer) complications years or decades later. The presence of eosinophilia is an important diagnostic clue.

Microbiology

Gastrointestinal & Nutrition

Schistosomiasis

Subject

System

Topic

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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 57-year-old man with a history of alcoholic cirrhosis is brought to the emergency department due to altered mental status. Over the weekend, he ate a lot of smoked meats at a local barbecue competition. Since then, he has been sleeping most of the day and is confused and disoriented when awake. On examination, he has abdominal distension with shifting dullness. The patient answers correctly when asked for his name but does not know that he is in the hospital and says the year is "1997." When asked to extend his hands as if stopping traffic, the patient makes rhythmic flapping movements. He is started on rifaximin. Which of the following is the most likely mechanism of action of this drug when used to treat this patient's current condition?

- ☐ A. Binding of dietary phosphate
- ☐ B. Decreased intraluminal ammonia production
- ☐ C. Exchange of intraluminal sodium ions for potassium ions
- ☐ D. Formation of a nonabsorbable complex with bile acids
- ☐ E. Increased conversion of ammonia to ammonium ion



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altered mental status. Over the weekend, he ate a lot of smoked meats at a local barbecue competition. Since then, he has been sleeping most of the day and is confused and disoriented when awake. On examination, he has abdominal distension with shifting dullness. The patient answers correctly when asked for his name but does not know that he is in the hospital and says the year is "1997." When asked to extend his hands as if stopping traffic, the patient makes rhythmic flapping movements. He is started on rifaximin. Which of the following is the most likely mechanism of action of this drug when used to treat this patient's current condition?

- ☐ A. Binding of dietary phosphate (1%)
- ☒ B. Decreased intraluminal ammonia production (47%)
- ☐ C. Exchange of intraluminal sodium ions for potassium ions (1%)
- ☐ D. Formation of a nonabsorbable complex with bile acids (3%)
- ☐ E. Increased conversion of ammonia to ammonium ion (45%)

Correct

47%



50 secs



09/12/2020

Block Time Remaining: 00:20:24

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Feedback



Suspend



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This patient likely has **hepatic encephalopathy** (HE), a neurologic complication of **cirrhosis** due in part to the liver's inability to convert **ammonia** (a neurotoxin) to urea. Excess ammonia is shunted past the liver and crosses the blood-brain barrier, leading to **altered mental status** (thought due to impaired neurotransmitter release, astrocyte dysfunction, neuroinflammation, and/or edema). Asterixis, the rhythmic flapping of dorsiflexed hands, is another common manifestation of HE.

A primary source of ammonia is degradation of nitrogen products by intestinal bacteria. Therefore, **gastrointestinal (GI) bleeding** can precipitate HE as hemoglobin breakdown leads to increased nitrogen products in the gut. **Excess dietary protein intake** (eg, large steak meal) is another common trigger. Others include infection, sedatives, and metabolic derangements (eg, hypokalemia).

**Rifaximin** is a nonabsorbable antibiotic that alters GI flora to decrease intestinal production and absorption of ammonia. In patients with HE, rifaximin is generally used in addition to **lactulose**, which is catabolized by intestinal bacterial flora to short chain fatty acids, lowering the colonic pH and increasing conversion of ammonia to ammonium (**Choice E**). Rifaximin is also sometimes used for traveler's diarrhea, as it inhibits bacterial RNA synthesis through binding with DNA-dependent RNA polymerase.

**(Choices A and C)** Phosphate binders (eg, calcium acetate) lower serum phosphate in patients with end-stage renal disease. Sodium polystyrene resin (eg, sodium polystyrene sulfonate) exchanges intraluminal







by intestinal bacterial flora to short chain fatty acids, lowering the colonic pH and increasing conversion of ammonia to ammonium (**Choice E**). Rifaximin is also sometimes used for traveler's diarrhea, as it inhibits bacterial RNA synthesis through binding with DNA-dependent RNA polymerase.

**(Choices A and C)** Phosphate binders (eg, calcium acetate) lower serum phosphate in patients with end-stage renal disease. Sodium polystyrene resin (eg, sodium polystyrene sulfonate) exchanges intraluminal sodium for potassium ions and can lower serum potassium in patients with hyperkalemia. However, neither effectively treats HE.

**(Choice D)** Bile acid sequestrants (cholestyramine, colestipol) bind intestinal bile acids to lower serum cholesterol, but they are not used for treating HE.

### Educational objective:

Treatments for hepatic encephalopathy include lactulose (increases conversion of ammonia to ammonium) and rifaximin (decreases intraluminal ammonia production).

### References

- [Treatment options for hepatic encephalopathy.](#)

Pharmacology

Gastrointestinal &amp; Nutrition

Cirrhosis

Subject

System

Topic

Block Time Remaining: 00:20:24

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0



Feedback



Suspend



End Block





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 75-year-old hospitalized man is evaluated for abdominal pain and fever. The patient was admitted 2 weeks ago due to necrotizing fasciitis of the gluteal region and severe sepsis. He has been treated with surgical debridements, intravenous antibiotics, and fluids. For the past 2 days, the patient has had right upper quadrant abdominal pain, nausea, and recurrent fever. He has a history of hypertension, type 2 diabetes mellitus, and chronic obstructive pulmonary disease. His temperature is 38.8 C (102 F). Physical examination shows marked tenderness over the right subcostal area. Leukocyte count is 18,000/mm<sup>3</sup> compared to 9,600/mm<sup>3</sup> 2 days ago. Laparoscopic surgery is planned. Which of the following will most likely be found during this patient's surgery?

- ☐ A. Choledochal cyst
- ☐ B. Fibrotic and shrunken gallbladder
- ☐ C. Fluke infection of the biliary tree
- ☐ D. Inflamed and enlarged gallbladder
- ☒ E. Pigment gallstones
- ☐ F. Porcelain gallbladder



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Suspend



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surgical debridements, intravenous antibiotics, and fluids. For the past 2 days, the patient has had right upper quadrant abdominal pain, nausea, and recurrent fever. He has a history of hypertension, type 2 diabetes mellitus, and chronic obstructive pulmonary disease. His temperature is 38.8 C (102 F). Physical examination shows marked tenderness over the right subcostal area. Leukocyte count is 18,000/mm<sup>3</sup> compared to 9,600/mm<sup>3</sup> 2 days ago. Laparoscopic surgery is planned. Which of the following will most likely be found during this patient's surgery?

- ☐ A. Choledochal cyst (2%)
- ☐ B. Fibrotic and shrunken gallbladder (1%)
- ☐ C. Fluke infection of the biliary tree (6%)
- ☒ D. Inflamed and enlarged gallbladder (71%)
- ☐ E. Pigment gallstones (13%)
- ☐ F. Porcelain gallbladder (4%)

Correct

71%  
Answered correctly02 mins, 14 secs  
Time spent11/15/2020  
Last updated

Block Time Remaining: 00:22:38

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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient likely has acute **acalculous cholecystitis**, an acute inflammation of the gallbladder in the absence of gallstones. Acalculous cholecystitis most commonly occurs in **critically ill** patients (eg, those with sepsis, severe burns, trauma, immunosuppression) and is associated with high mortality. The condition is thought to arise secondary to gallbladder stasis and **ischemia**, which cause inflammation of and injury to the gallbladder wall.

Clinical manifestations may be subtle, especially in those who are sedated or intubated. **Fever, right upper quadrant pain**, a positive Murphy's sign, **leukocytosis**, and mild elevations in liver function tests are often present. Physical examination may demonstrate jaundice and a palpable right upper quadrant mass. The diagnostic study of choice is an ultrasound, which may show signs of acute cholecystitis (eg, an edematous and enlarged gallbladder) and **no gallstones**.

**(Choice A)** Choledochal cysts are congenital dilations of the common bile duct that typically present during childhood (age <10) with recurrent abdominal pain and jaundice.

**(Choice B)** Chronic cholecystitis results from repeated mild attacks of acute cholecystitis, which leads to thickening of the gallbladder wall. Ultrasound typically demonstrates a shrunken, fibrosed gallbladder.

**(Choice C)** Liver fluke infection usually affects individuals from endemic areas (eg, Southeast Asia) and presents acutely with fever, right upper quadrant pain, jaundice, and eosinophilia. Infection of the biliary



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



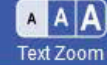
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thickening of the gallbladder wall. Ultrasound typically demonstrates a shrunken, fibrosed gallbladder.

**(Choice C)** Liver fluke infection usually affects individuals from endemic areas (eg, Southeast Asia) and presents acutely with fever, right upper quadrant pain, jaundice, and eosinophilia. Infection of the biliary tree is associated with the formation of brown pigment gallstones, not acute acalculous cholecystitis.

**(Choice E)** Pigment gallstones are categorized as black (typically secondary to intravascular hemolysis) or brown (typically secondary to biliary infection). These gallstones are associated with acute calculous cholecystitis, not acute acalculous cholecystitis.

**(Choice F)** Porcelain gallbladder is usually found incidentally on abdominal radiograph as a rim of calcium deposits outlining the gallbladder. The condition is associated with chronic cholecystitis and may increase the risk of gallbladder carcinoma.

### Educational objective:

Acute acalculous cholecystitis is an acute inflammation of the gallbladder in the absence of gallstones. It typically occurs in critically ill patients (eg, those with sepsis, severe burns, trauma, immunosuppression) due to gallbladder stasis and ischemia. Clinical findings may be subtle and include fever, right upper quadrant pain, and leukocytosis.

### References

Block Time Remaining: 00:22:38

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 56-year-old man comes to the emergency department because of sudden onset of severe, diffuse abdominal pain. The patient has experienced 3 months of epigastric pain that has been refractive to proton-pump inhibitor therapy. Physical examination reveals an exquisitely tender, rigid abdomen with rebound tenderness. Abdominal radiographs reveal free air under the diaphragm. Supportive therapy is initiated. Exploratory laparotomy reveals a large, perforated gastric ulcer with features suggestive of malignancy. He undergoes partial gastrectomy with gastrojejunostomy. Long-term supplementation with which of the following is most important in this patient?

- ☐ A. Ascorbic acid
- ☐ B. Biotin
- ☐ C. Iron
- ☐ D. Pantothenic acid
- ☐ E. Pyridoxine

**Submit**

Block Time Remaining: 00:22:39

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1



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Settings

A 56-year-old man comes to the emergency department because of sudden onset of severe, diffuse abdominal pain. The patient has experienced 3 months of epigastric pain that has been refractive to proton-pump inhibitor therapy. Physical examination reveals an exquisitely tender, rigid abdomen with rebound tenderness. Abdominal radiographs reveal free air under the diaphragm. Supportive therapy is initiated. Exploratory laparotomy reveals a large, perforated gastric ulcer with features suggestive of malignancy. He undergoes partial gastrectomy with gastrojejunostomy. Long-term supplementation with which of the following is most important in this patient?

- ☐ A. Ascorbic acid (4%)
- ☐ B. Biotin (4%)
- ☒ C. Iron (74%)
- ☐ D. Pantothenic acid (4%)
- ☐ E. Pyridoxine (12%)







Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 56-year-old man comes to the emergency department because of sudden onset of severe, diffuse abdominal pain. The patient has experienced 3 months of epigastric pain that has been refractive to proton-pump inhibitor therapy. Physical examination reveals an exquisitely tender, rigid abdomen with rebound tenderness. Abdominal radiographs reveal free air under the diaphragm. Supportive therapy is initiated. Exploratory laparotomy reveals a large, perforated gastric ulcer with features suggestive of malignancy. He undergoes partial gastrectomy with gastrojejunostomy. Long-term supplementation with which of the following is most important in this patient?

- ☐ A. Ascorbic acid (4%)
- ☐ B. Biotin (4%)
- ☒ C. Iron (74%)
- ☐ D. Pantothenic acid (4%)
- ☐ E. Pyridoxine (12%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



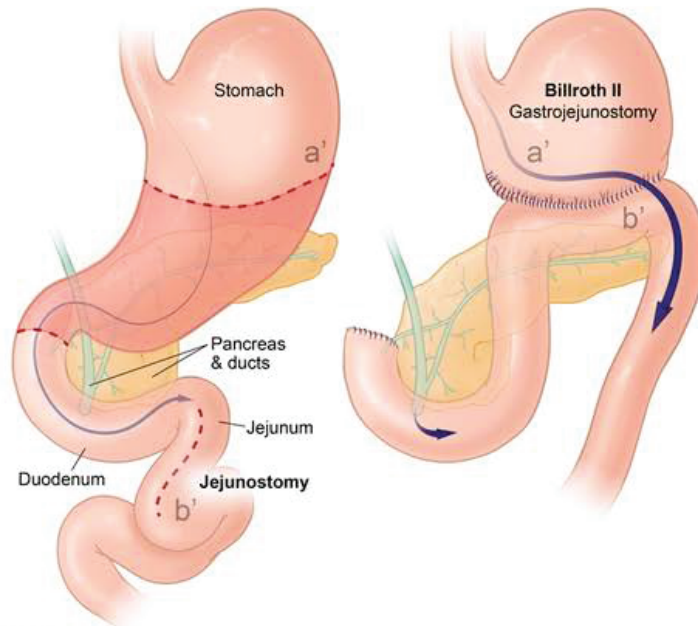
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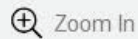
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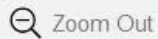
## Billroth II



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Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Partial gastrectomy with **gastrojejunostomy** is most often performed to treat **complicated peptic ulcer disease** (eg, perforation, malignancy, gastric outlet obstruction) or ulcers refractory to medical management. In a Billroth II gastrojejunostomy, the gastric antrum is removed to decrease gastrin production and for histopathologic evaluation. A side-to-side anastomosis is then made between the jejunum and the gastric body, bypassing the duodenum and proximal jejunum.

**Iron absorption** occurs predominantly in the **duodenum and proximal jejunum**, and bypass of this segment of small bowel results in iron deficiency **anemia**. The post-surgical decrease in gastric acidity also diminishes iron absorption and may contribute to iron deficiency in these patients. Treatment is accomplished with pharmacologic **iron supplementation**, which allows for adequate iron absorption at secondary absorption sites in the distal small bowel.

Deficiency involving thiamine, folate, vitamin B<sub>12</sub>, fat-soluble vitamins (especially vitamin D), and calcium is also common following gastrojejunostomy.

**(Choice A)** Although ascorbic acid (vitamin C) can increase the bioavailability of nonheme iron, vitamin C supplementation would not be enough to counteract the effect of decreased iron absorption post-gastrojejunostomy.

**(Choices B and D)** Biotin (vitamin B<sub>7</sub>) and pantothenic acid (vitamin B<sub>5</sub>) are absorbed in the small and







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice A)** Although ascorbic acid (vitamin C) can increase the bioavailability of nonheme iron, vitamin C supplementation would not be enough to counteract the effect of decreased iron absorption post-gastrojejunostomy.

**(Choices B and D)** Biotin (vitamin B<sub>7</sub>) and pantothenic acid (vitamin B<sub>5</sub>) are absorbed in the small and large intestine via the sodium-dependent multivitamin transporter. Deficiency of either of these vitamins is rare and not associated with gastric bypass procedures.

**(Choice E)** Pyridoxine (vitamin B<sub>6</sub>) absorption occurs in the jejunum and the ileum by passive diffusion and is not typically affected by gastrojejunostomy.

### Educational objective:

Iron absorption occurs predominantly in the duodenum and proximal jejunum. Bypass of this segment of small bowel by gastrojejunostomy results in iron deficiency anemia that can be corrected with pharmacologic iron supplementation. Malabsorption of thiamine, folate, vitamin B<sub>12</sub>, fat-soluble vitamins (especially vitamin D), and calcium is also common following gastric bypass procedures.

Pharmacology

Gastrointestinal &amp; Nutrition

Iron deficiency anemia

Subject

System

Topic

Block Time Remaining: 00:23:22

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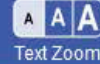
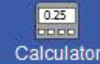
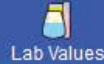
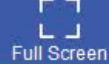
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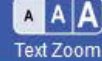
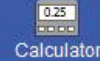
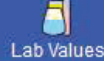
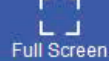
A 34-year-old man is evaluated for elevated liver aminotransferases. The patient has no chronic medical conditions but has a history of injection drug use. Family history is notable for liver cirrhosis in his mother. Ultrasonography-guided liver biopsy is performed. Histopathology demonstrates marked panlobular mononuclear cell infiltration that cross into adjacent lobules. Occasional intensely eosinophilic round bodies are seen scattered amongst the hepatic parenchyma. Which of the following is the most likely cause of the latter histopathological finding in this patient?

- ☐ A. Coagulative necrosis due to a toxin
- ☐ B. Cytotoxic T-cell-mediated apoptosis
- ☐ C. Intracellular pigment accumulation
- ☐ D. Intracytoplasmic cyokeratin deposition
- ☐ E. Small foci of fibrinoid necrosis
- ☐ F. Stellate cell activation into myofibroblast

**Submit**

Block Time Remaining: 00:23:23

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A 34-year-old man is evaluated for elevated liver aminotransferases. The patient has no chronic medical conditions but has a history of **injection** drug use. Family history is notable for liver cirrhosis in his mother. Ultrasonography-guided liver biopsy is performed. Histopathology demonstrates marked panlobular mononuclear cell infiltration that cross into adjacent lobules. Occasional intensely eosinophilic round bodies are seen scattered amongst the hepatic parenchyma. Which of the following is the most likely cause of the latter histopathological finding in this patient?

- ☐ A. Coagulative necrosis due to a toxin (5%)
- ✓ ☒ B. Cytotoxic T-cell-mediated apoptosis (44%)
- ☐ C. Intracellular pigment accumulation (7%)
- ☐ D. Intracytoplasmic cytokeratin deposition (19%)
- ☐ E. Small foci of fibrinoid necrosis (9%)
- ☐ F. Stellate cell activation into myofibroblast (13%)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



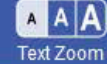
Notes



Calculator



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Text Zoom



Settings

This patient who has a history of intravenous drug use likely has elevated aminotransferases due to **acute viral hepatitis**. Most cases are marked by significant **panlobular lymphocytic inflammation**, which may "bridge" into adjacent hepatic lobules due to collapse of the reticulin framework. Spotty areas of hepatocyte injury are typically seen. Necrotic hepatocytes appear ballooned with pale cytoplasm (ballooning degeneration). Alternatively, hepatocytes may undergo **cytotoxic T-cell-mediated apoptosis** due to the presence of viral antigens on the hepatocyte surface. These apoptotic cells appear as round, acidophilic (pink on hematoxylin and eosin staining) bodies known as **Councilman bodies**.

Unlike acute viral hepatitis, chronic viral hepatitis is usually characterized by significant inflammation surrounding the portal triad (hepatic artery branch, portal vein branch, bile ductule). Hepatocytes usually have a ground-glass appearance (chronic hepatitis B virus) or an abundance of fat (chronic hepatitis C virus). Intravenous drug use is tightly linked to the transmission of hepatitis B and C virus.

**(Choice A)** Toxin-mediated hepatic injury (eg, due to acetaminophen) usually results in centrilobular hepatocyte necrosis (ie, centered around central veins) due to oxidative damage.

**(Choice C)** Hemochromatosis is characterized by the deposition of **iron** within hepatocytes, which results in the cells appearing pigmented when stained with Prussian blue. There is no fibrosis or inflammatory



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Feedback



Suspend



End Block



hepatocyte necrosis (ie, centered around central veins) due to oxidative damage.

**(Choice C)** Hematochromatosis is characterized by the deposition of **iron** within hepatocytes, which results in the cells appearing pigmented when stained with Prussian blue. There is no fibrosis or inflammatory infiltrate.

**(Choice D)** **Mallory bodies** are damaged cytokeratin filaments within hepatocytes that usually arise in patients with alcoholism. They appear as highly eosinophilic inclusions on microscopy. Alcohol-mediated liver injury is associated with fat deposition in hepatocytes, particularly in the centrilobular region.

**(Choice E)** Aschoff bodies are small areas of granulomatous inflammation seen in the myocardium of patients with rheumatic heart disease. They are not seen in the liver.

**(Choice F)** Stellate cells reside in the hepatic perisinusoidal space and can transdifferentiate into myofibroblasts in response to liver injury; they are the primary cells associated with liver fibrosis. However, this patient has an inflammatory infiltrate and Councilman bodies, not fibrosis.

**Educational objective:**

Intravenous drug use is a major risk factor for hepatitis B and C viral infection. Acute viral hepatitis is marked by panlobular inflammation and hepatocyte necrosis and ballooning. Cytotoxic T-cell-mediated signals also cause hepatocyte apoptosis with the formation of intensely eosinophilic Councilman bodies.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 45-year-old woman comes to the office due to several months of episodic right upper quadrant abdominal pain associated with nausea. The pain is often brought on by fatty meals and subsides in 1-2 hours. The patient has no fever, vomiting, diarrhea, melena, or bright red blood per rectum. Her BMI is 31.2 kg/m<sup>2</sup>. Physical examination is unremarkable. A cholecystokinin stimulation test is performed and shows slow and incomplete gallbladder emptying. This patient is most likely to have which of the following pathologic findings?

- ☐ A. Biliary sludge
- ☐ B. Black pigment stones
- ☐ C. Brown pigment stones
- ☐ D. Cystine stones
- ☐ E. Uric acid stones

**Submit**

Block Time Remaining: 00:25:35

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom





Settings

A 45-year-old woman comes to the office due to several months of episodic right upper quadrant abdominal pain associated with nausea. The pain is often brought on by fatty meals and subsides in 1-2 hours. The patient has no fever, vomiting, diarrhea, melena, or bright red blood per rectum. Her BMI is 31.2 kg/m<sup>2</sup>. Physical examination is unremarkable. A cholecystokinin stimulation test is performed and shows slow and incomplete gallbladder emptying. This patient is most likely to have which of the following pathologic findings?

- ☒ A. Biliary sludge (50%)
- ☐ B. Black pigment stones (16%)
- ☐ C. Brown pigment stones (30%)
- ☐ D. Cystine stones (1%)
- ☐ E. Uric acid stones (0%)

Correct

 50%  
Answered correctly 46 secs  
Time Spent 08/31/2020  
Last Updated

Block Time Remaining: 00:26:20

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



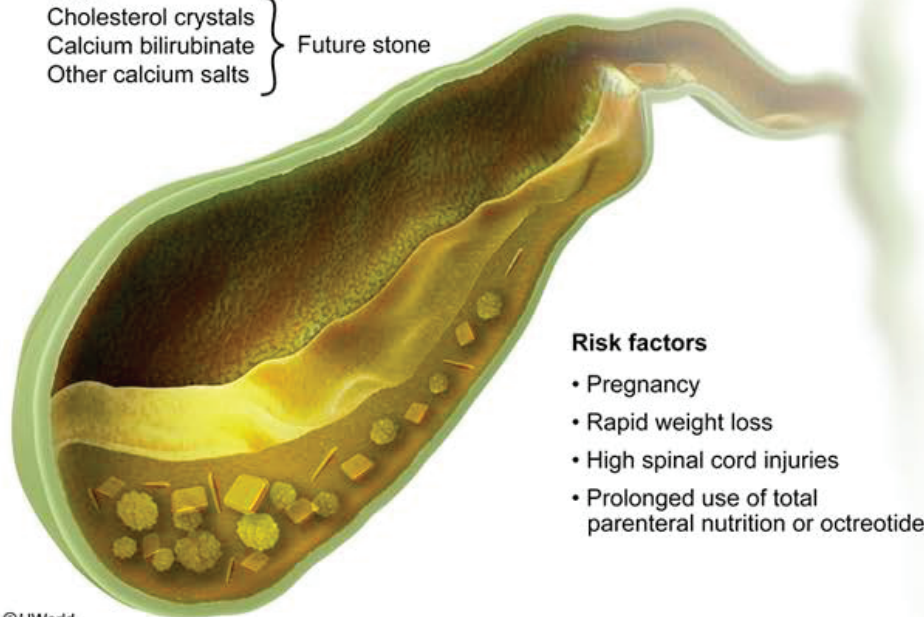
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## Exhibit Display

## Biliary sludge

Mucin  
Cholesterol crystals  
Calcium bilirubinate  
Other calcium salts

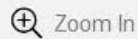
Future stone



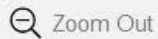
## Risk factors

- Pregnancy
- Rapid weight loss
- High spinal cord injuries
- Prolonged use of total parenteral nutrition or octreotide

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Reset



New



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1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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This patient's slow/incomplete gallbladder emptying in response to cholecystokinin stimulation is consistent with **gallbladder hypomotility**. The gallbladder functions to actively absorb water from bile; conditions that cause gallbladder hypomotility result in excessive dehydration of bile. This promotes the precipitation and accumulation of particulate material (eg, cholesterol monohydrate crystals, calcium bilirubinate, mucus) in bile, forming viscous **biliary sludge**. Sludge formation may be asymptomatic or cause biliary colic (right upper quadrant abdominal pain associated with nausea) and is a known precursor to stone formation (particularly cholesterol stones). Complications such as acute cholecystitis and cholangitis can also occur in patients with biliary sludge.

**(Choices B and C)** Pigment gallstones can be brown or black and arise from conditions that increase the amount of unconjugated bilirubin in bile. Brown pigment stones are associated with biliary tract infections (microbes producing  $\beta$ -glucuronidases), whereas black stones occur with chronic hemolytic anemias (eg, sickle cell disease) and increased enterohepatic cycling of bilirubin (eg, Crohn disease, which also decreases enterohepatic cycling of bile acids). This patient has no risk factors for pigment stones, and her gallbladder dysmotility makes biliary sludge a more likely diagnosis.

**(Choice D)** Cystinuria is an autosomal recessive condition characterized by a defect in an amino acid

Block Time Remaining: 00:26:20

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice D)** Cystinuria is an autosomal recessive condition characterized by a defect in an amino acid transporter gene, resulting in elevated urinary cystine concentrations. Patients typically present with cystine kidney stones during childhood or adolescence.

**(Choice E)** Individuals with high serum uric acid levels are at increased risk of developing uric acid kidney stones. Hyperuricemia can be caused by uric acid underexcretion (eg, thiazide diuretics) or overproduction (eg, tumor lysis syndrome).

### Educational objective:

The gallbladder functions to actively absorb water from bile. Gallbladder hypomotility causes the bile to become concentrated, promoting precipitation and accumulation of particulate material. This forms a viscous biliary sludge that can cause transient bile duct obstruction (biliary colic) and promote cholesterol gallstone formation.

### References

- Biliary sludge: the sluggish gallbladder.
- Gallbladder sludge: what is its clinical significance?
- Lithogenesis and bile metabolism.



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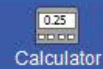
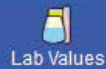
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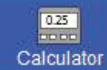
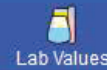
A 10-year-old boy is brought to the hospital for difficulty swallowing. During dinner a few hours ago, a piece of chicken became stuck in the patient's mid-chest region. His parents say that he has previously had the sensation of food becoming stuck, but it has never lasted this long. The patient has vomited multiple times, but the chicken has not dislodged. Medical history is significant for eczema. He is drooling and visibly uncomfortable. An upper endoscopy is performed to remove the chicken from the esophagus, which exhibits multiple stacked, circular, ringlike indentations; linear furrowing; and scattered, small, whitish papules. Which of the following findings is most likely to be seen on biopsy of this patient's esophagus?

- ☐ A. Eosinophilic infiltration of the esophageal mucosa
- ☐ B. Ganglionic degeneration within the myenteric plexus
- ☐ C. Intestinal metaplasia of the esophageal epithelium
- ☐ D. Replacement of the esophagus with fibrous tissue
- ☐ E. Squamous cells with eosinophilic intranuclear inclusions

**Submit**

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A 10-year-old boy is brought to the hospital for difficulty swallowing. During dinner a few hours ago, a piece of chicken became stuck in the patient's mid-chest region. His parents say that he has previously had the sensation of food becoming stuck, but it has never lasted this long. The patient has vomited multiple times, but the chicken has not dislodged. Medical history is significant for eczema. He is drooling and visibly uncomfortable. An upper endoscopy is performed to remove the chicken from the esophagus, which exhibits multiple stacked, circular, ringlike indentations; linear furrowing; and scattered, small, whitish papules. Which of the following findings is most likely to be seen on biopsy of this patient's esophagus?

- ☒ A. Eosinophilic infiltration of the esophageal mucosa (56%)
- ☐ B. Ganglionic degeneration within the myenteric plexus (11%)
- ☐ C. Intestinal metaplasia of the esophageal epithelium (2%)
- ☐ D. Replacement of the esophagus with fibrous tissue (15%)
- ☐ E. Squamous cells with eosinophilic intranuclear inclusions (13%)





### Eosinophilic esophagitis

<b>Pathogenesis</b>	<ul style="list-style-type: none"><li>• Chronic Th2 cell-mediated disorder triggered by food antigens</li><li>• Eosinophilic infiltration of the esophageal mucosa</li></ul>
<b>Epidemiology</b>	<ul style="list-style-type: none"><li>• Men &gt; women</li><li>• History of atopic conditions</li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• Intermittent dysphagia</li><li>• Reflux, vomiting, chest or abdominal pain</li><li>• Esophageal food impaction</li></ul>

**Th2** = T helper 2.

This patient with a history of solid food dysphagia has an esophageal food impaction due to **eosinophilic esophagitis** (EOE). EOE is a chronic Th2 cell-mediated disorder triggered by food antigen exposure. When activated, Th2 cells release chemokines (eg, IL-13, IL-5) that stimulate eosinophilic recruitment to the esophageal mucosa.

EOE is most common in males with a history of **atopic conditions** (eg, eczema, asthma). Patients often



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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EOE is most common in males with a history of **atopic conditions** (eg, eczema, asthma). Patients often have **intermittent solid food dysphagia**. Other symptoms include vomiting, reflux, and chest and upper abdominal pain. When EOE is severe, food can become trapped in the esophagus (ie, **esophageal food impaction**), requiring urgent upper endoscopy to remove the impacted food bolus.

Classic endoscopic findings include stacked, circular, **ringlike indentations**; **linear furrowing**; and scattered, small, whitish papules (ie, **eosinophilic microabscesses**). Biopsies demonstrate **eosinophilic mucosal infiltration**.

**(Choice B)** Achalasia results from ganglionic degeneration within the esophageal myenteric plexus, leading to the inability to relax the lower esophageal sphincter. It typically causes dysphagia of both solids and liquids and is rare in children. There are no specific endoscopic findings; however, a barium swallow demonstrating a **bird-beak appearance** of the esophagus is characteristic.

**(Choice C)** Barrett esophagus is a premalignant condition characterized by intestinal metaplasia of the esophageal epithelium. It typically develops in older patients with uncontrolled gastroesophageal reflux but does not usually cause food impaction.

**(Choice D)** Systemic sclerosis results in esophageal smooth muscle fibrosis, leading to severe gastroesophageal reflux. It occurs more commonly in adult women and usually presents with thickened



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**(Choice C)** Barrett esophagus is a premalignant condition characterized by intestinal metaplasia of the esophageal epithelium. It typically develops in older patients with uncontrolled gastroesophageal reflux but does not usually cause food impaction.

**(Choice D)** Systemic sclerosis results in esophageal smooth muscle fibrosis, leading to severe gastroesophageal reflux. It occurs more commonly in adult women and usually presents with thickened skin and Raynaud phenomenon. Endoscopy typically demonstrates a dilated esophagus.

**(Choice E)** Herpes simplex virus esophagitis is characterized histologically by eosinophilic intranuclear inclusions within esophageal squamous cells. It typically occurs in immunocompromised patients and results in severe odynophagia. Endoscopy demonstrates ulcerations with a volcano-like appearance.

### Educational objective:

Eosinophilic esophagitis is a Th2 cell-mediated disorder leading to eosinophilic infiltration of the esophageal mucosa. It occurs most commonly in males with a history of atopic conditions and typically presents with solid food dysphagia, reflux, and occasionally food impaction. Classic endoscopic findings include stacked, circular, ringlike indentations; linear furrowing; and scattered, small, whitish papules (ie, eosinophilic microabscesses).

### References







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Previous



Next



Full Screen



Tutorial



Lab Values



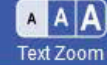
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A 53-year-old female treated with high-dose folic acid for anemia experiences a moderate increase in her hemoglobin level. She returns to clinic complaining of bilateral foot numbness and difficulty in walking. The latter symptoms are most likely related to which of the following?

- ☐ A. Folate overdose
- ☐ B. Iron deficiency
- ☐ C. Cobalamin deficiency
- ☐ D. Hemolysis
- ☐ E. Aplastic anemia

**Submit**

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Feedback



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color




Text Zoom



Settings

A 53-year-old female treated with high-dose folic acid for anemia experiences a moderate increase in her hemoglobin level. She returns to clinic complaining of bilateral foot numbness and difficulty in walking. The latter symptoms are most likely related to which of the following?

- ☐ A. Folate overdose (4%)
- ☐ B. Iron deficiency (1%)
- ☒ C. Cobalamin deficiency (90%)
- ☐ D. Hemolysis (1%)
- ☐ E. Aplastic anemia (1%)

**Correct** 90%  
Answered correctly 21 secs  
Time Spent 02/17/2021  
Last Updated

Explanation

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Feedback



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The clinical decision to treat this patient with folic acid suggests that her anemia was megaloblastic and therefore likely secondary to a deficiency in folate and/or vitamin B<sub>12</sub> (cobalamin). Her subsequent development of neurological symptoms (a finding not associated with folate deficiency alone) indicates that she is deficient in vitamin B<sub>12</sub>.

A moderate improvement in the hemoglobin level often occurs when a deficiency in vitamin B<sub>12</sub> is treated with folate, or vice versa. However, the treatment of vitamin B<sub>12</sub> deficiency with folate will not reverse any neurologic dysfunction caused by the vitamin B<sub>12</sub> deficiency. In fact, the usage of folate alone can worsen demyelination and cause abnormal myelin synthesis by depleting the concentration of unmethylated cobalamin available for methylmalonyl-CoA processing. The walking difficulties and paresthesias seen in this patient were therefore likely precipitated by the administration of folate alone.

**(Choice A)** High doses of folate may antagonize phenytoin, thereby precipitating seizures in a select group of patients. Walking difficulties and paresthesias are not typically associated with folate overdose, however.

**(Choice B)** Iron deficiency is characterized by a hypochromic, microcytic anemia that is best treated with







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice A)** High doses of folate may antagonize phenytoin, thereby precipitating seizures in a select group of patients. Walking difficulties and paresthesias are not typically associated with folate overdose, however.

**(Choice B)** Iron deficiency is characterized by a hypochromic, microcytic anemia that is best treated with iron supplementation. Walking difficulties and paresthesias are not typically associated with iron deficiency anemia.

**(Choices D and E)** Anemia of any cause can provoke nonspecific neurologic symptoms (eg, tinnitus, irritability, generalized weakness). Walking difficulties and paresthesias are not commonly associated with hemolysis or aplastic anemia, however.

### Educational Objective:

Deficiency of vitamin B<sub>12</sub> is associated with both megaloblastic anemia and neurologic dysfunction, while folate deficiency is associated with megaloblastic anemia alone. Moderate improvement in the hemoglobin level often occurs when a deficiency in vitamin B<sub>12</sub> is treated with folate, or vice versa. Treatment of vitamin B<sub>12</sub> deficiency with folate alone can actually worsen neurologic dysfunction.

Pathology

Gastrointestinal &amp; Nutrition

Vitamin b12 deficiency

Block Time Remaining: 00:28:12

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Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

An 18-year-old man is admitted to the hospital with cough, fever, and hypoxemia. Despite multiple intravenous antibiotics and frequent chest physiotherapy, the patient decompensates and is transferred to the intensive care unit for mechanical ventilation. Sputum cultures grow >100,000 colony-forming units of a non-lactose-fermenting gram-negative rod. After several days, the patient dies of overwhelming pneumonia complicated by respiratory failure. Since age 1, he had been hospitalized for recurrent episodes of multi-lobar pneumonia, sinusitis, and poor growth. On autopsy, both vas deferens are absent. Which of the following findings is also likely to be present on autopsy?

- ☐ A. Distension and obstruction of pancreatic ducts
- ☐ B. Lobar sequestration
- ☐ C. Lymphocytic infiltrate of pancreatic islet cells
- ☒ D. Nodular lymphoid hyperplasia in the intestine
- ☐ E. Situs inversus

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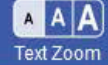
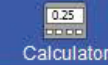
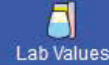
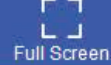
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An 18-year-old man is admitted to the hospital with cough, fever, and hypoxemia. Despite multiple intravenous antibiotics and frequent chest physiotherapy, the patient decompensates and is transferred to the intensive care unit for mechanical ventilation. Sputum cultures grow >100,000 colony-forming units of a non-lactose-fermenting gram-negative rod. After several days, the patient dies of overwhelming pneumonia complicated by respiratory failure. Since age 1, he had been hospitalized for recurrent episodes of multi-lobar pneumonia, sinusitis, and poor growth. On autopsy, both vas deferens are absent. Which of the following findings is also likely to be present on autopsy?

- ☒ A. Distension and obstruction of pancreatic ducts (69%)
- ☐ B. Lobar sequestration (1%)
- ☐ C. Lymphocytic infiltrate of pancreatic islet cells (3%)
- ☐ D. Nodular lymphoid hyperplasia in the intestine (1%)
- ☐ E. Situs inversus (24%)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Clinical features of cystic fibrosis

<b>Respiratory</b>	<ul style="list-style-type: none"><li>• Obstructive lung disease → bronchiectasis</li><li>• Recurrent pneumonia</li><li>• Chronic rhinosinusitis</li></ul>
<b>Gastrointestinal</b>	<ul style="list-style-type: none"><li>• Obstruction (10%-20%)<ul style="list-style-type: none"><li>◦ Meconium ileus</li><li>◦ Distal intestinal obstruction syndrome</li></ul></li><li>• Pancreatic disease<ul style="list-style-type: none"><li>◦ Exocrine pancreatic insufficiency</li><li>◦ CF-related diabetes (~25%)</li></ul></li><li>• Biliary cirrhosis</li></ul>
<b>Reproductive</b>	<ul style="list-style-type: none"><li>• Infertility (&gt;95% men, ~20% women)</li></ul>
<b>Musculoskeletal</b>	<ul style="list-style-type: none"><li>• Osteopenia → fractures</li><li>• Kyphoscoliosis</li><li>• Digital clubbing</li></ul>

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Cystic fibrosis transmembrane conductance regulator (CFTR) normally allows for transport of chloride into

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Cystic fibrosis transmembrane conductance regulator (CFTR) normally allows for transport of chloride into gastrointestinal and respiratory lumens, followed by sodium and water, leading to thin mucus. In cystic fibrosis (CF), the dysfunctional or absent *CFTR* gene leads to decreased water within the lumen, resulting in **thick, dehydrated, and viscous mucus** within organs.

This patient's **recurrent sinopulmonary infections** and **congenital absence of the vas deferens** are consistent with CF. Pneumonia due to a non-lactose-fermenting, gram-negative rod (*Pseudomonas aeruginosa* or *Burkholderia cepacia*) is very common.

The most common gastrointestinal manifestation of CF is **pancreatic insufficiency (PI)**. Pancreatic duct obstruction and distension due to viscous mucus and subsequent inflammation develop in utero, eventually leading to fibrosis. PI is present from birth in most patients with CF. The loss of pancreatic tissue prevents these patients from developing pancreatitis. PI results in inability to absorb fats and fat-soluble vitamins (ADEK), leading to **steatorrhea** and **failure to thrive**. Patients with PI require **pancreatic enzyme supplementation**.

**(Choice B)** Bronchopulmonary sequestration is a congenital malformation characterized by extra, nonfunctional lung tissue without communication to the tracheobronchial tree. The extra tissue can be within a lung lobe or outside of the lungs and can present as recurrent pneumonia in the same focal site.



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice B)** Bronchopulmonary sequestration is a congenital malformation characterized by extra,

nonfunctional lung tissue without communication to the tracheobronchial tree. The extra tissue can be within a lung lobe or outside of the lungs and can present as recurrent pneumonia in the same focal site.

**(Choice C)** Lymphocytic infiltration of pancreatic islet cells is seen in the pathogenesis of type 1 diabetes mellitus. One or more autoantigens within these cells serves as a target for autoimmune attack, eventually leading to destruction of insulin-producing pancreatic cells.

**(Choice D)** Nodular lymphoid hyperplasia of the intestine is classically seen in common variable immunodeficiency syndrome (CVID), a disorder of low immunoglobulin and B lymphocyte levels that predisposes to recurrent sinopulmonary and gastrointestinal infections. Congenital absence of the vas deferens is not associated with CVID.

**(Choice E)** Situs inversus refers to transposition of the major internal organs (eg, dextrocardia). It is associated with primary ciliary dyskinesia (or Kartagener syndrome), in which inefficient cilia in multiple organs fail to beat synchronously and clear mucus. Recurrent sinopulmonary infections and bronchiectasis result, but absence of the vas deferens does not occur.

### Educational objective:

The most common gastrointestinal disorder in patients with cystic fibrosis is pancreatic insufficiency.

Block Time Remaining: 00:28:54

<https://t.me/USMLEWorldStep1>



Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice D)** Nodular lymphoid hyperplasia of the intestine is classically seen in common variable immunodeficiency syndrome (CVID), a disorder of low immunoglobulin and B lymphocyte levels that predisposes to recurrent sinopulmonary and gastrointestinal infections. Congenital absence of the vas deferens is not associated with CVID.

**(Choice E)** Situs inversus refers to transposition of the major internal organs (eg, dextrocardia). It is associated with primary ciliary dyskinesia (or Kartagener syndrome), in which inefficient cilia in multiple organs fail to beat synchronously and clear mucus. Recurrent sinopulmonary infections and bronchiectasis result, but absence of the vas deferens does not occur.

### Educational objective:

The most common gastrointestinal disorder in patients with cystic fibrosis is pancreatic insufficiency. Mutations in the cystic fibrosis transmembrane conductance regulator gene lead to thick, viscous secretions in the lumens of the pancreas, resulting in obstruction, inflammation, and subsequent fibrosis. Clinical manifestations include steatorrhea, failure to thrive, and deficiency of fat-soluble vitamins.

### References

- Cystic fibrosis.
- Gastrointestinal disorders in cystic fibrosis.



Feedback



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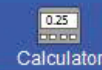
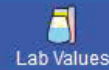


A 69-year-old man is evaluated for abdominal pain. Upper gastrointestinal endoscopy shows a single shallow, 1-cm ulcer in the duodenal bulb and mild gastric erythema. Biopsy specimens from the gastric antrum do not show *Helicobacter pylori*, and stool testing for *H pylori* antigen is negative. Which of the following parts of the history is most likely to reveal the cause of this patient's current condition?

- ☐ A. Family history
- ☐ B. Food diary
- ☐ C. Medication use
- ☐ D. Recent travel
- ☐ E. Seasonal allergies

Submit





A 69-year-old man is evaluated for abdominal pain. Upper gastrointestinal endoscopy shows a single shallow, 1-cm ulcer in the duodenal bulb and mild gastric erythema. Biopsy specimens from the gastric antrum do not show *Helicobacter pylori*, and stool testing for *H pylori* antigen is negative. Which of the following parts of the history is most likely to reveal the cause of this patient's current condition?

- ☐ A. Family history (13%)
- ☐ B. Food diary (6%)
- ☒ C. Medication use (76%)
- ☐ D. Recent travel (2%)
- ☐ E. Seasonal allergies (0%)

Correct

76%  
Answered correctly

40 secs  
Time Spent

02/08/2021  
Last Updated

Explanation

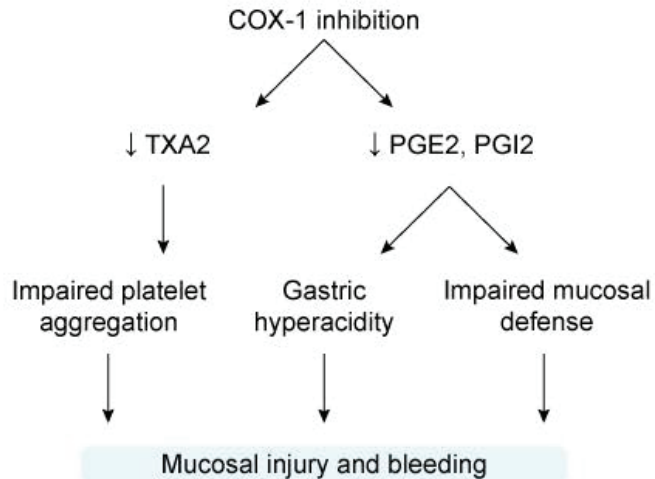
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## Explanation

**NSAID-induced gastrointestinal bleeding**

COX-1 = cyclo-oxygenase type 1; PGE2 = prostaglandin E2;  
PGI2 = prostaglandin I2 (prostacyclin); TXA2 = thromboxane A2.

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**Peptic ulcers** (defects in the stomach or duodenal mucosa) are most commonly due to *Helicobacter pylori*



**Peptic ulcers** (defects in the stomach or duodenal mucosa) are most commonly due to *Helicobacter pylori* infection or **nonsteroidal anti-inflammatory drug (NSAID) use**. The majority of duodenal ulcers are associated with *H pylori* infection, but the prevalence is decreasing in the United States due to improved hygienic practices. *H pylori* has been adequately ruled out in this patient; therefore, he most likely has an NSAID-related duodenal ulcer.

Nonselective NSAIDs (eg, ibuprofen, naproxen, aspirin) exert analgesic, anti-inflammatory, and antipyretic effects through the inhibition of both forms of the cyclo-oxygenase (COX) enzyme. In the gastrointestinal tract, the COX-1 subtype is responsible for the synthesis of prostaglandins, which are critical for the maintenance of intestinal mucosa. **Inhibition of COX-1** leads to increased gastric acid formation, decreased mucosal bicarbonate production, and decreased mucosal blood flow, which can increase the risk for gastritis and peptic ulcer formation. Patients who are age >65 or those on long-term or high-dose NSAID therapy are at the highest risk.

**(Choice A)** Multiple endocrine neoplasia type 1 is a rare hereditary disorder that presents with pituitary, parathyroid, and pancreatic tumors, including gastrinomas. Gastrinomas manifest as peptic ulcer disease, but patients typically develop multiple ulcers and often have evidence of other neoplasias (eg, hypercalcemia from hyperparathyroidism, visual field defects from pituitary adenomas).

**(Choice B and E)** Diet and seasonal allergies are not associated with peptic ulcer disease, although





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

parathyroid, and pancreatic tumors, including gastrinomas. Gastrinomas manifest as peptic ulcer disease, but patients typically develop multiple ulcers and often have evidence of other neoplasias (eg, hypercalcemia from hyperparathyroidism, visual field defects from pituitary adenomas).

**(Choices B and E)** Diet and seasonal allergies are not associated with peptic ulcer disease, although certain foods (eg, spicy) may exacerbate ulcer-related dyspepsia and abdominal pain.

**(Choice D)** Travel to a resource-limited country increases the risk of *H pylori* infection; however, *H pylori* was ruled out in this patient.

### Educational objective:

Peptic ulcers are most commonly caused by *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug (NSAID) use. NSAIDs inhibit cyclo-oxygenase-1, leading to increased gastric acid formation, decreased mucosal bicarbonate production, and decreased mucosal blood flow, which promote mucosal injury and ulcer formation.

Pathology

Gastrointestinal &amp; Nutrition

Peptic ulcer disease

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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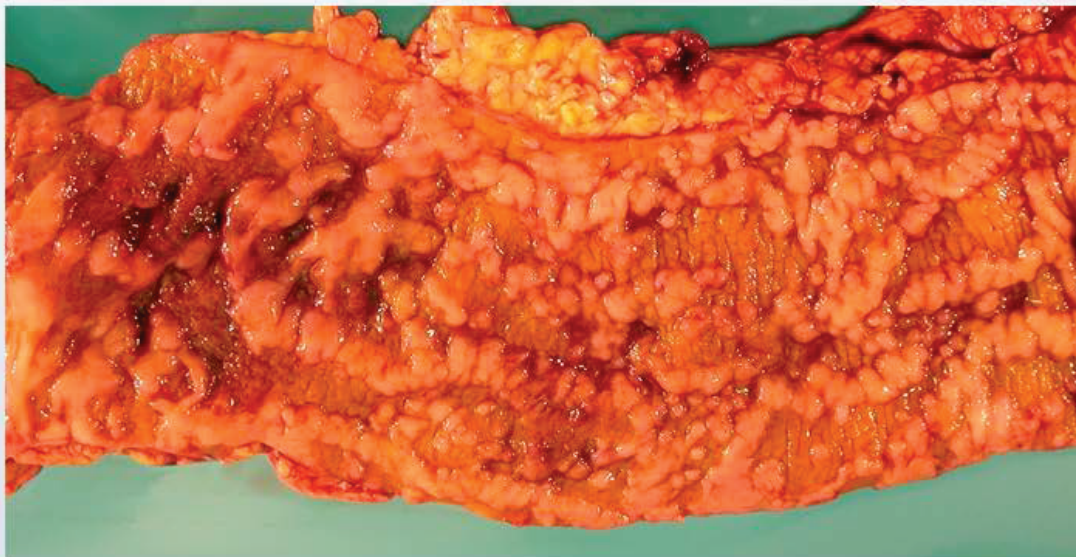


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Settings

A 24-year-old woman comes to the office due to recurrent bloody diarrhea and right-sided abdominal pain. She has had these symptoms intermittently for several years but has not sought medical attention until now. Colonoscopy shows evidence of inflammation and dysplasia. The patient is started on appropriate medical therapy but her symptoms fail to respond adequately. She subsequently undergoes a colectomy of the involved region; findings are shown in the image.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



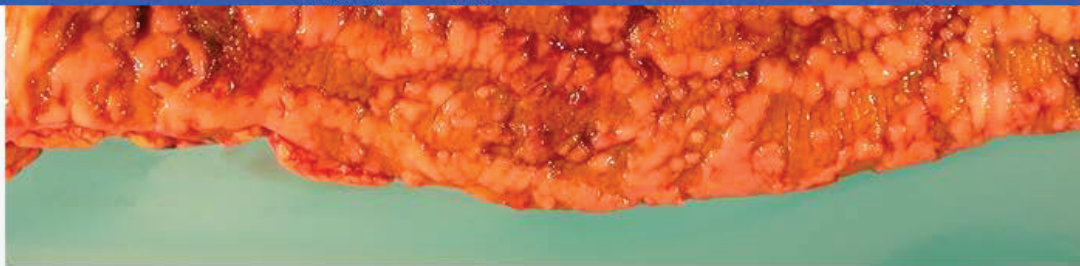
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Settings



The intestinal wall appears thickened. Which of the following is the most likely diagnosis?

- ☐ A. Amoebic dysentery
- ☐ B. Collagenous microscopic colitis
- ☐ C. Crohn disease
- ☐ D. Graft-versus-host disease
- ☐ E. Pseudomembranous colitis
- ☐ F. Ulcerative colitis

**Submit**

Block Time Remaining: 00:29:41

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



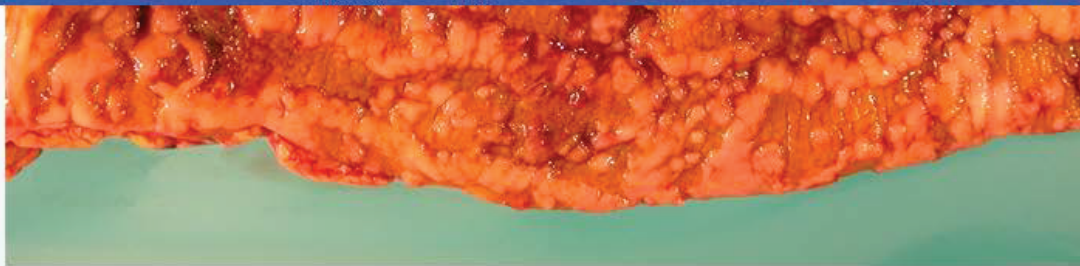
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The intestinal wall appears thickened. Which of the following is the most likely diagnosis?

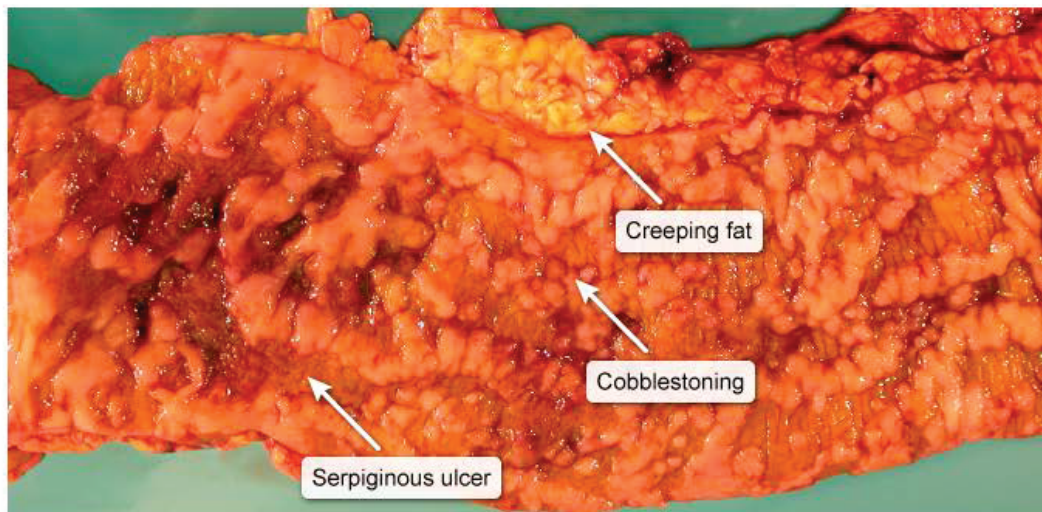
- ☐ A. Amoebic dysentery (0%)
- ☐ B. Collagenous microscopic colitis (2%)
- ☒ C. Crohn disease (60%)
- ☐ D. Graft-versus-host disease (0%)
- ☐ E. Pseudomembranous colitis (2%)
- ☐ F. Ulcerative colitis (35%)





## Explanation

## Crohn disease



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**Crohn disease (CD)** is an inflammatory bowel disease characterized by patchy inflammation that can

Block Time Remaining: 00:29:47

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Feedback

Suspend

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Mark

Previous

Next

Serpiginous ulcer

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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**Crohn disease** (CD) is an inflammatory bowel disease characterized by patchy inflammation that can occur throughout the entire gastrointestinal (GI) tract; patients commonly complain of relapsing and remitting abdominal pain, diarrhea (with or without blood), and weight loss. CD typically involves the ileum; however, up to 20% of patients have only colonic involvement. Unlike ulcerative colitis, which is characterized by continuous inflammation of the colon limited to the mucosa and submucosa, inflammation in CD is **transmural** (full thickness) and **segmental** in nature. This leads to recognizable manifestations on gross pathology, including:

- **Skip lesions** – sharply delineated ulcerations surrounded by normal bowel
- **Cobblestone** appearance – serpiginous (ie, wavy, snakelike) depressed ulcerations that separate elevated islands of healthy tissue (giving the mucosa an appearance of a cobblestone street)
- **Bowel wall thickening** – due to inflammation involving all layers of the bowel wall leading to edema, hypertrophy of the muscularis mucosa, and fibrosis
- **Creeping fat** – mesenteric fat becomes wrapped around the bowel, possibly in response to intestinal bacteria translocation





Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom

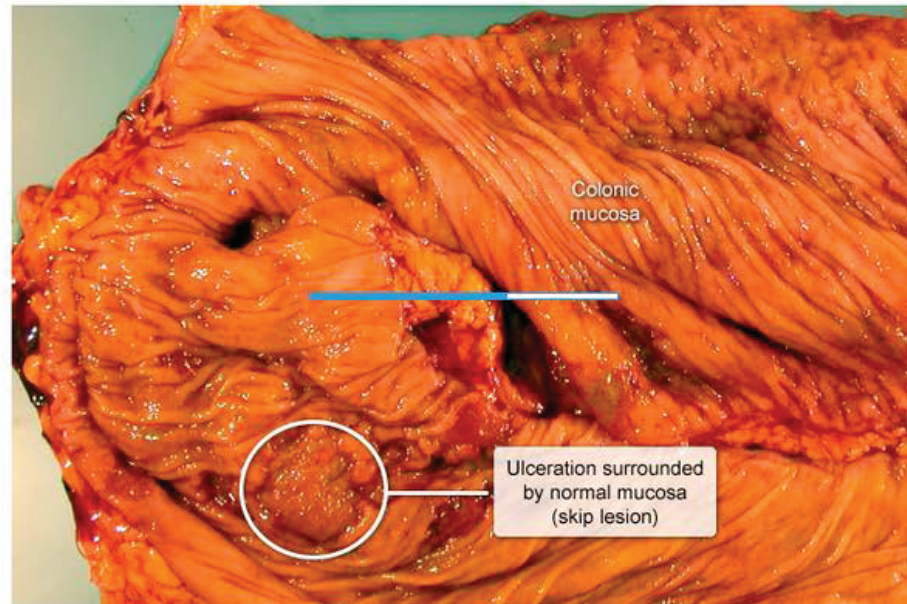


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Serpiginous ulcer

## Exhibit Display

## Crohn disease



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Block Time Remaining: 00:29:47

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End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

## bacteria translocation

In addition, the transmural inflammation frequently leads to complications such as abscesses, **strictures**, and **fistulas**.

**(Choice A)** Amoebic dysentery caused by *Entamoeba histolytica* causes hematochezia, abdominal pain, and ulcerations; however, the ulcers are classically flask-shaped and smaller than those seen with inflammatory bowel disease.

**(Choice B)** Collagenous colitis can cause chronic watery diarrhea (>5-10 episodes daily) but is commonly seen in middle-aged women and is not associated with bleeding, ulcerations, inflammation, or abdominal pain.

**(Choice D)** Graft-versus-host disease of the GI tract can cause abdominal pain and ulcerations, but it typically causes severe diarrhea (up to 10 L daily) and occurs as a complication of allogeneic stem cell transplant.

**(Choice E)** Pseudomembranous colitis occurs from *Clostridioides difficile* infection (CDI). It causes abdominal pain and diarrhea that can result in toxic megacolon. A white/yellow, patchy pseudomembrane, composed of inflammatory cells, fibrin, and cellular debris, is often visualized. In addition, CDI is typically associated with recent antibiotic use.



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice E)** *Pseudomembranous colitis* occurs from *Clostridioides difficile* infection (CDI). It causes abdominal pain and diarrhea that can result in toxic megacolon. A white/yellow, patchy pseudomembrane, composed of inflammatory cells, fibrin, and cellular debris, is often visualized. In addition, CDI is typically associated with recent antibiotic use.

**(Choice F)** *Ulcerative colitis* is characterized by contiguous inflammation that extends from the rectum. Ulcerations are shallow and involve only the mucosa and submucosa; pseudopolyps (areas of inflamed mucosa and/or granulation tissue that appear polyp-like due to surrounding ulcerations) are seen; bowel wall thickening is not as prominent as with CD.

### Educational objective:

Crohn disease is an inflammatory bowel disease characterized by patchy inflammation that can occur throughout the entire gastrointestinal tract. Gross pathology demonstrates skip lesions, cobblestoning of the mucosa, bowel wall thickening, and creeping fat.

Pathology

Gastrointestinal &amp; Nutrition

Inflammatory bowel disease

Subject

System

Topic

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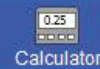
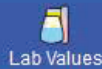
Feedback



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A 62-year-old woman comes to the office for diarrhea. She has had 4 or 5 watery, brown stools every day for the past 6 months. Although most episodes occur during the day, she wakes up at least once a night to defecate. There is no associated hematochezia, melena, vomiting, or unexpected weight loss. Medical history is significant for type 2 diabetes mellitus and hypertension. She takes lisinopril, insulin, and metformin. She has no recent travel or new medications. Family history is unremarkable. She does not drink alcohol. Temperature is 37.4 C (99.3 F), blood pressure is 125/80 mm Hg, and pulse is 80/min. The abdomen is nontender and nondistended. Complete blood count, serum chemistries, and stool studies are normal. Which of the following is the most likely cause of this patient's diarrhea?

- ☐ A. Decreased bacterial growth in the colon
- ☐ B. Disaccharidase deficiency
- ☐ C. Disordered motility of the small bowel and colon
- ☐ D. Exocrine pancreatic insufficiency
- ☐ E. Transmural intestinal inflammation







for the past 6 months. Although most episodes occur during the day, she wakes up at least once a night to defecate. There is no associated hematochezia, melena, vomiting, or unexpected weight loss. Medical history is significant for type 2 diabetes mellitus and hypertension. She takes lisinopril, insulin, and metformin. She has no recent travel or new medications. Family history is unremarkable. She does not drink alcohol. Temperature is 37.4 C (99.3 F), blood pressure is 125/80 mm Hg, and pulse is 80/min. The abdomen is nontender and nondistended. Complete blood count, serum chemistries, and stool studies are normal. Which of the following is the most likely cause of this patient's diarrhea?

- ☐ A. Decreased bacterial growth in the colon (7%)
- ☐ B. Disaccharidase deficiency (14%)
- ☒ C. Disordered motility of the small bowel and colon (55%)
- ☐ D. Exocrine pancreatic insufficiency (15%)
- ☐ E. Transmural intestinal inflammation (6%)

Correct



55%

Answered correctly



01 min, 23 secs

Time Spent



12/23/2020

Last Updated

Block Time Remaining: 00:31:10

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1



Feedback



Suspend



End Block

### Diabetic diarrhea

<b>Etiology</b>	<ul style="list-style-type: none"><li>• Long-standing hyperglycemia damages the autonomic nervous system, resulting in:<ul style="list-style-type: none"><li>◦ Altered intestinal motility</li><li>◦ Increased intestinal secretions</li><li>◦ ± Fecal incontinence</li></ul></li></ul>
<b>Risk factors</b>	<ul style="list-style-type: none"><li>• Poorly controlled diabetes mellitus</li><li>• Vascular risk factors (eg, smoking, obesity, hyperlipidemia)</li></ul>
<b>Manifestations</b>	<ul style="list-style-type: none"><li>• Painless, watery diarrhea</li><li>• Secretory-like (persists at night &amp; while fasting)</li><li>• Laboratory evaluation typically unremarkable</li></ul>

This patient with diabetes mellitus has several months of watery diarrhea that occurs both during the day and at night. In the setting of normal laboratory evaluation, this presentation suggests **diabetic diarrhea** due to **diabetic autonomic neuropathy** (DAN). Long-standing hyperglycemia results in the accumulation of cross-linked glycosylated serum proteins in the vasa nervorum, which causes inflammation and **damage**



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

• Laboratory evaluation typically unremarkable

This patient with diabetes mellitus has several months of watery diarrhea that occurs both during the day and at night. In the setting of normal laboratory evaluation, this presentation suggests **diabetic diarrhea** due to **diabetic autonomic neuropathy** (DAN). Long-standing hyperglycemia results in the accumulation of cross-linked glycosylated serum proteins in the vasa nervorum, which causes inflammation and **damage to peripheral nerves**. Although this most commonly results in a distal, symmetric polyneuropathy of the feet, it can also result in damage to **sympathetic and parasympathetic nerves**, leading to autonomic dysfunction. Risk factors include poor glucose control and other vascular risk factors (eg, hypertension, obesity).

Loss of autonomic input to the gastrointestinal tract results in abnormal peristalsis, leading to **disordered small-bowel and colonic motility**, which can result in rapid intestinal transport. Furthermore, intestinal water and electrolyte secretion is increased. **Fecal incontinence** is particularly common in patients with long-standing diabetes, resulting from both a large volume of watery diarrhea and decreased anorectal sensation. Other common gastrointestinal manifestations of DAN include gastroparesis and gastroesophageal reflux.

Patients with diabetic diarrhea typically have painless, secretory-like diarrhea that **persists with fasting** (eg, nocturnal diarrhea). Laboratory evaluation, including fecal leukocytes and fecal occult blood testing, is

Block Time Remaining: 00:31:10

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(eg, nocturnal diarrhea). Laboratory evaluation, including fecal leukocytes and fecal occult blood testing, is usually unremarkable.

**(Choice A)** Although altered small-bowel motility related to DAN can predispose to small intestinal bacterial overgrowth, this occurs due to an increase in small bowel bacteria, not a decrease in colonic bacterial burden. It typically causes abdominal bloating, discomfort, and gas. Nocturnal diarrhea is unexpected.

**(Choice B)** Lactase deficiency can cause osmotic diarrhea after lactose ingestion, leading to postprandial loose stools and bloating. However, unless patients are eating during the night, nocturnal bowel movements would not occur.

**(Choice D)** Exocrine pancreatic insufficiency (EPI), which is common in chronic pancreatitis or after pancreatic resection, leads to bulky, foul-smelling stool (eg, steatorrhea). Although insulin resistance can mildly impact pancreatic secretions, EPI leading to steatorrhea is rare in diabetes.

**(Choice E)** Crohn disease, which causes transmural gastrointestinal inflammation, can cause watery diarrhea. However, abdominal pain, anemia, abnormal stool studies (eg, fecal occult blood, fecal calprotectin), and possibly fever are expected.

Educational Objective:

Block Time Remaining: 00:31:10

<https://t.me/USMLEWorldStep1>



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Feedback



Suspend



End Block



loose stools and bloating. However, unless patients are eating during the night, nocturnal bowel movements would not occur.

**(Choice D)** Exocrine pancreatic insufficiency (EPI), which is common in chronic pancreatitis or after pancreatic resection, leads to bulky, foul-smelling stool (eg, steatorrhea). Although insulin resistance can mildly impact pancreatic secretions, EPI leading to steatorrhea is rare in diabetes.

**(Choice E)** Crohn disease, which causes transmural gastrointestinal inflammation, can cause watery diarrhea. However, abdominal pain, anemia, abnormal stool studies (eg, fecal occult blood, fecal calprotectin), and possibly fever are expected.

### Educational objective:

Prolonged hyperglycemia in diabetes mellitus can injure the parasympathetic and sympathetic nervous system, resulting in diabetic autonomic neuropathy. This can lead to disordered small-bowel and colonic motility and increased intestinal secretions, resulting in secretory-like diarrhea (eg, fasting bowel movements).

Pathophysiology

Gastrointestinal & Nutrition

Diabetic neuropathy

Subject

System

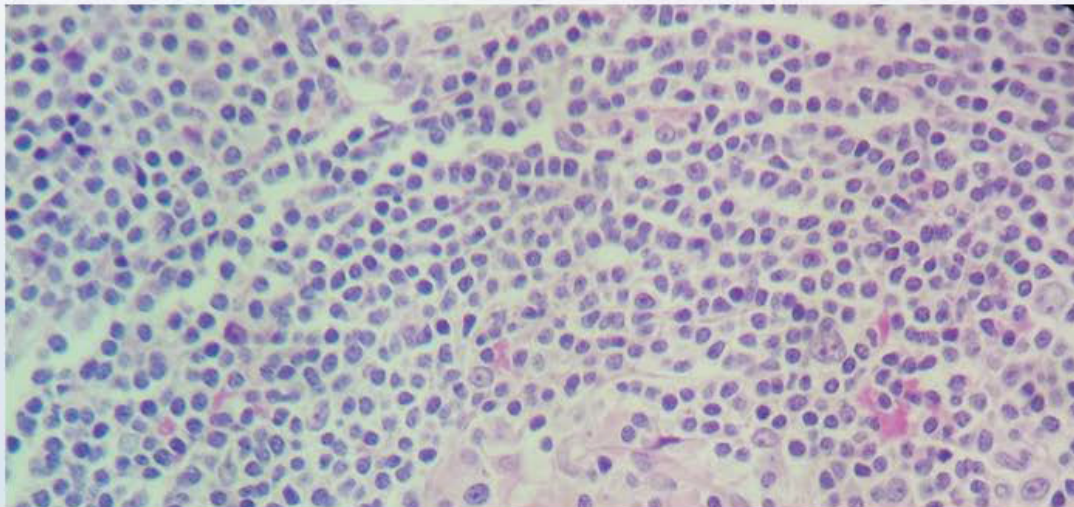
Topic

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A 28-year-old man comes to the emergency department due to progressive abdominal pain. Although he has had mild abdominal cramps in the past, he has never before experienced anything this severe. The patient has 8-10 watery stools a day, weight loss, fatigue, and lethargy. Temperature is 38.3 C (100.9 F), blood pressure is 125/82 mm Hg, pulse is 95/min, and respirations are 14/min. The abdomen is tender to palpation without rebound or guarding. Abdominal CT scan reveals inflammatory changes affecting the ascending colon, sigmoid colon, and terminal ileum. Intestinal biopsy reveals the following:







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

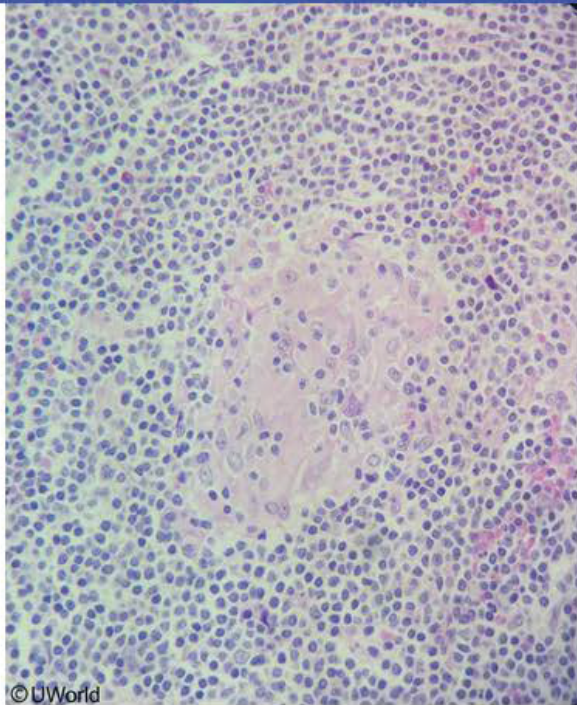


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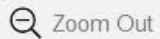
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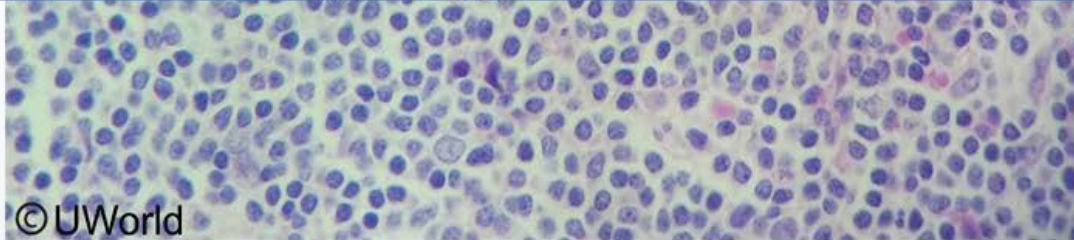
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Effective treatment of this patient's condition could be achieved by targeting which of the following molecules?

- ☐ A. BCR-ABL protein tyrosine kinase
- ☐ B. CD20 lymphocyte antigen
- ☐ C. mTOR protein kinase
- ☐ D. Programmed cell death-1 protein
- ☐ E. Tumor necrosis factor-alpha

Submit

Block Time Remaining: 00:31:20

<https://t.me/USMLEWorldStep1>





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



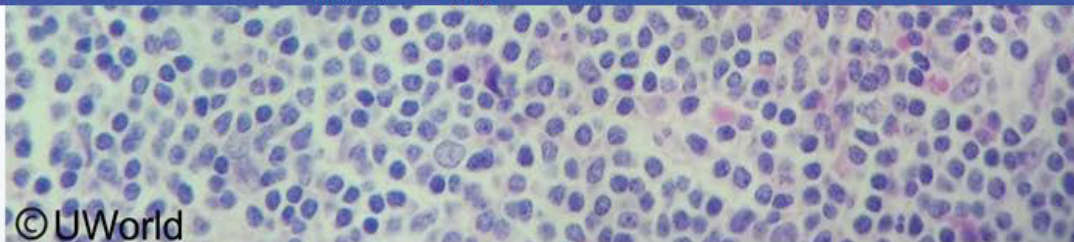
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Text Zoom



Settings



Effective treatment of this patient's condition could be achieved by targeting which of the following molecules?

- ☐ A. BCR-ABL protein tyrosine kinase (3%)
- ☐ B. CD20 lymphocyte antigen (9%)
- ☐ C. mTOR protein kinase (6%)
- ☐ D. Programmed cell death-1 protein (3%)
- ☒ E. Tumor necrosis factor-alpha (77%)

Correct



77%

Answered correctly



01 min, 16 secs

Time spent



10/04/2020

Last updated

Block Time Remaining: 00:32:26

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Feedback



Suspend



End Block



### Crohn disease

#### Involvement

- Extending from the mouth to the anus (mostly ileum & colon)
- Rectum spared
- Perianal disease
- Skip lesions

#### Microscopy

- Noncaseating granulomas

#### Gross findings

- Transmural inflammation
- Linear mucosal ulcerations
- Cobblestoning
- Creeping fat

#### Clinical manifestations

- Diarrhea (bloody if colitis)

#### Intestinal complications

- Fistulae
- Strictures (bowel obstruction)
- Abscesses



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient with recurrent abdominal pain, diarrhea, weight loss, and low-grade fevers has inflammatory changes of the colon and terminal ileum. In association with the characteristic intestinal biopsy findings, this presentation is consistent with **Crohn disease** (CD). CD is an inflammatory bowel disease that causes **patchy inflammation** throughout the gastrointestinal (GI) tract but spares the rectum; patients typically have segments of normal bowel interspersed with areas of disease (skip lesions).

The presence of **noncaseating granulomas** on intestinal biopsy is highly suggestive of CD. These lesions are characterized by the accumulation of epithelioid macrophages that fuse to form multinucleated cells surrounded by a band of lymphocytes. Other characteristic histopathologic findings in CD include inflammation involving the entire thickness of the intestinal wall (transmural inflammation), distortion of normal mucosal architecture, and Paneth cell metaplasia.

**Tumor necrosis factor-alpha** (TNF- $\alpha$ ), an inflammatory cytokine produced by macrophages, plays a central role in the pathogenesis of CD. It **promotes intestinal inflammation** by inducing lymphocyte proliferation, enhancing migration of neutrophils into the GI tract, and stimulating macrophage activity. Several TNF- $\alpha$  inhibitors (eg, infliximab, adalimumab) are used as first-line therapy in the treatment of CD.

**(Choice A)** Chronic myeloid leukemia (CML) occurs from a translocation between chromosomes 9 and 22, leading to creation of the BCR-ABL (fusion) protein tyrosine kinase. Imatinib, a direct inhibitor of BCR-ABL

Block Time Remaining: 00:32:26

<https://t.me/USMLEWorldStep1>



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



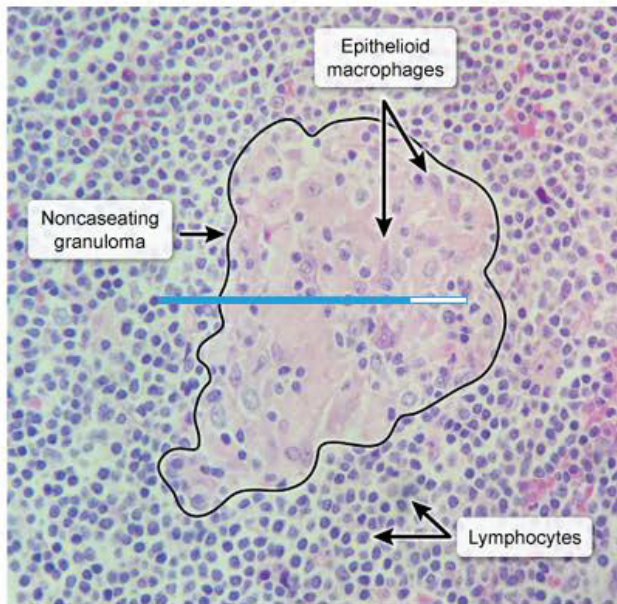
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Settings

## Exhibit Display

## Crohn disease



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Reset

New | Existing

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leading to creation of the BCR-ABL (fusion) protein tyrosine kinase. Imatinib, a direct inhibitor of BCR-ABL

Block Time Remaining: 00:32:26

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block





Several TNF- $\alpha$  inhibitors (eg, infliximab, adalimumab) are used as first-line therapy in the treatment of CD.

**(Choice A)** Chronic myeloid leukemia (CML) occurs from a translocation between chromosomes 9 and 22, leading to creation of the BCR-ABL (fusion) protein tyrosine kinase. Imatinib, a direct inhibitor of BCR-ABL, is effective for CML but not for CD.

**(Choice B)** CD20 antigen is specific to B lymphocytes. Rituximab, a monoclonal antibody directed at CD20, results in B cell depletion. It is used in multiple autoimmune disorders (eg, rheumatoid arthritis) but not CD.

**(Choice C)** mTOR (mammalian target of rapamycin) is a stimulator of cell growth and proliferation. Sirolimus, an mTOR inhibitor, is used in patients with solid organ transplants to prevent allograft rejection.

**(Choice D)** Programmed cell death-1 (PD-1) is an immune checkpoint molecule that downregulates the immune response. PD-1 inhibitors (eg, nivolumab, pembrolizumab) are cancer immunotherapy drugs used to stimulate the immune response against malignant cells.

### Educational objective:

Crohn disease is an inflammatory bowel disorder that causes patchy inflammation throughout the gastrointestinal tract. Characteristic histopathologic findings include noncaseating granulomas, transmural inflammation, and Paneth cell metaplasia. Tumor necrosis factor-alpha (TNF- $\alpha$ ), a cytokine produced by





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice B)** CD20 antigen is specific to B lymphocytes. Rituximab, a monoclonal antibody directed at CD20, results in B cell depletion. It is used in multiple autoimmune disorders (eg, rheumatoid arthritis) but not CD.

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### Educational objective:

Crohn disease is an inflammatory bowel disorder that causes patchy inflammation throughout the gastrointestinal tract. Characteristic histopathologic findings include noncaseating granulomas, transmural inflammation, and Paneth cell metaplasia. Tumor necrosis factor-alpha (TNF- $\alpha$ ), a cytokine produced by macrophages, plays a central role in the pathogenesis of CD; anti-TNF- $\alpha$  agents (eg, infliximab, adalimumab) are often used as first-line therapy.

### References

- [Role of cytokines in the pathogenesis of inflammatory bowel disease](#)

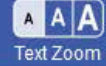
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Feedback

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End Block



A 45-year-old Caucasian male presents to your office with a two year history of abdominal discomfort, greasy stool and weight loss. He has been treated for joint pain with ibuprofen. After initial work-up, an intestinal biopsy shows multiple macrophages loaded with PAS-positive granules in the lamina propria.

This patient should be treated with:

- ☐ A. Enzyme supplementation
- ☐ B. Antibiotics
- ☐ C. Special diet
- ☐ D. Parenteral nutrition
- ☐ E. Aminosalicyclic acid derivates
- ☐ F. Surgical resection

Submit

Block Time Remaining: 00:32:27

<https://t.me/USMLEWorldStep1>



Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 45-year-old Caucasian male presents to your office with a two year history of abdominal discomfort, greasy stool and weight loss. He has been treated for joint pain with ibuprofen. After initial work-up, an intestinal biopsy shows multiple macrophages loaded with PAS-positive granules in the lamina propria.

This patient should be treated with:

- ☐ A. Enzyme supplementation (7%)
- ☒ B. Antibiotics (64%)
- ☐ C. Special diet (16%)
- ☐ D. Parenteral nutrition (1%)
- ☐ E. Aminosalicyclic acid derivates (5%)
- ☐ F. Surgical resection (4%)

Correct



64%

Answered correctly



28 secs

Time Spent



01/30/2021

Last Updated

Block Time Remaining: 00:32:54

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Caused by the gram-positive actinomycete *Tropheryma whippellii*, Whipple disease is a rare systemic illness that involves the small intestine, joints, and central nervous system. The actinomycete proliferates only within the macrophages of these tissues, provoking no inflammatory response as a consequence. Classic histologic findings include small intestine mucosa containing enlarged, foamy macrophages packed with both rod-shaped bacilli and PAS-positive, diastase-resistant granules (which consist of lysosomes and partially digested bacteria).

Clinically, Whipple disease is most commonly seen in middle-aged Caucasian males, presenting as malabsorption with diarrhea and weight loss. Arthropathy, polyarthritis, and psychiatric and cardiac abnormalities may also be observed. Antibiotic therapy is usually successful in quickly resolving the illness.

**(Choice A)** Digestive enzyme supplementation is appropriate for patients with diminished exocrine pancreatic function.

**(Choice C)** A special diet is appropriate for patients with celiac sprue or other food-sensitive conditions.

**(Choice D)** Parenteral nutrition is appropriate for all patients in need of prolonged bowel rest, such as those suffering from acute pancreatitis.

**(Choice E)** Aminosalicyclic acid derivatives are appropriate in treating ulcerative colitis.

Block Time Remaining: 00:32:54

<https://t.me/USMLEWorldStep1>

0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

(Choice C) A special diet is appropriate for patients with celiac sprue or other food-sensitive conditions.

(Choice D) Parenteral nutrition is appropriate for all patients in need of prolonged bowel rest, such as those suffering from acute pancreatitis.

(Choice E) Aminosalicilyc acid derivates are appropriate in treating ulcerative colitis.

(Choice F) Surgery is appropriate for patients with bowel conditions not responsive to medical treatment (eg, severe diverticulitis, ischemic bowel).

### Educational Objective:

Caused by the gram-positive actinomycete *Tropheryma whippelii*, Whipple disease is a rare systemic illness that involves the small intestine, joints, and central nervous system. Classic histologic findings include small intestine mucosa containing enlarged, foamy macrophages packed with both rod-shaped bacilli and PAS-positive, diastase-resistant granules.

Pathology

Gastrointestinal &amp; Nutrition

Whipple disease

Subject

System

Topic

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Block Time Remaining: 00:32:54

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0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

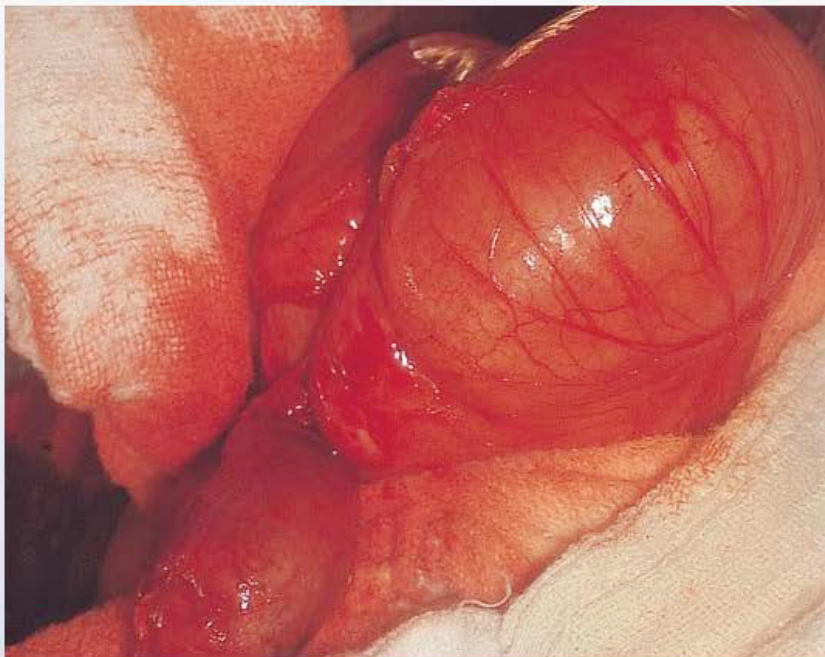


Text Zoom



Settings

A 22-year-old Caucasian male presents to the ER with abdominal pain that started around his bellybutton, then moved to the right lower abdominal quadrant. After initial evaluation, laparotomy is performed, which reveals the following findings (see the slide below).



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



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Which of the following most likely initiated this patient's condition?

- ☐ A. Bacterial infection
- ☐ B. Peptic ulceration
- ☐ C. Lumen obstruction
- ☐ D. Venous thrombosis
- ☐ E. Arterial spasm



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



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Which of the following most likely initiated this patient's condition?

- ☐ A. Bacterial infection (19%)
- ☐ B. Peptic ulceration (1%)
- ☒ C. Lumen obstruction (74%)
- ☐ D. Venous thrombosis (2%)
- ☐ E. Arterial spasm (1%)

Correct

74%



16 secs



01/30/2021

Block Time Remaining: 00:33:10

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Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

An inflamed, hyperemic, and edematous appendix is shown above. This macroscopic appearance, along with periumbilical pain that migrates to the right lower quadrant, is classic for acute appendicitis. This condition occurs in all age groups, with peak incidence in children 6-10 years old. The abdominal pain tends to appear in the periumbilical area (visceral pain) and shifts to the right lower quadrant a few hours later.

Acute appendicitis is caused by an obstruction of the appendicular lumen. The most common obstructing agents are fecaliths. Obstruction by hyperplastic lymphoid follicles, foreign bodies, nematodes, and carcinoids may also cause acute appendicitis. Retained mucus causes the appendicular wall to distend, which impairs venous outflow. The resulting hypoxia causes ischemia and associated bacterial invasion. Inflammation and edema of the appendicular wall occur, causing further distention. Necrosis of the wall with rupture may follow. In this case, inflammatory fluid and bacterial contents spill into the peritoneal cavity, causing peritonitis.

**(Choice A)** Bacterial infection plays an important role in the pathogenesis of acute appendicitis. It is not, however, the initiating event.

**(Choice B)** Peptic ulceration is implicated in the development of lower intestinal bleeding due to Meckel diverticulum, not acute appendicitis.



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

with rupture may follow. In this case, inflammatory fluid and bacterial contents spill into the peritoneal cavity, causing peritonitis.

**(Choice A)** Bacterial infection plays an important role in the pathogenesis of acute appendicitis. It is not, however, the initiating event.

**(Choice B)** Peptic ulceration is implicated in the development of lower intestinal bleeding due to Meckel diverticulum, not acute appendicitis.

**(Choices D and E)** Both venous thrombosis and arterial spasm can cause mesenteric ischemia; however, neither of these factors lead to acute appendicitis.

### Educational Objective:

Obstruction of the lumen of the appendix is the first event in pathogenesis of acute appendicitis. Fecaliths, hyperplastic lymphoid follicles, foreign bodies, or tumors may cause the obstruction. Right lower quadrant abdominal pain, nausea, vomiting, diarrhea, and fever are the typical manifestations of acute appendicitis.

Pathology

Gastrointestinal &amp; Nutrition

Appendicitis

Subject

System

Topic

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Block Time Remaining: 00:33:10

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

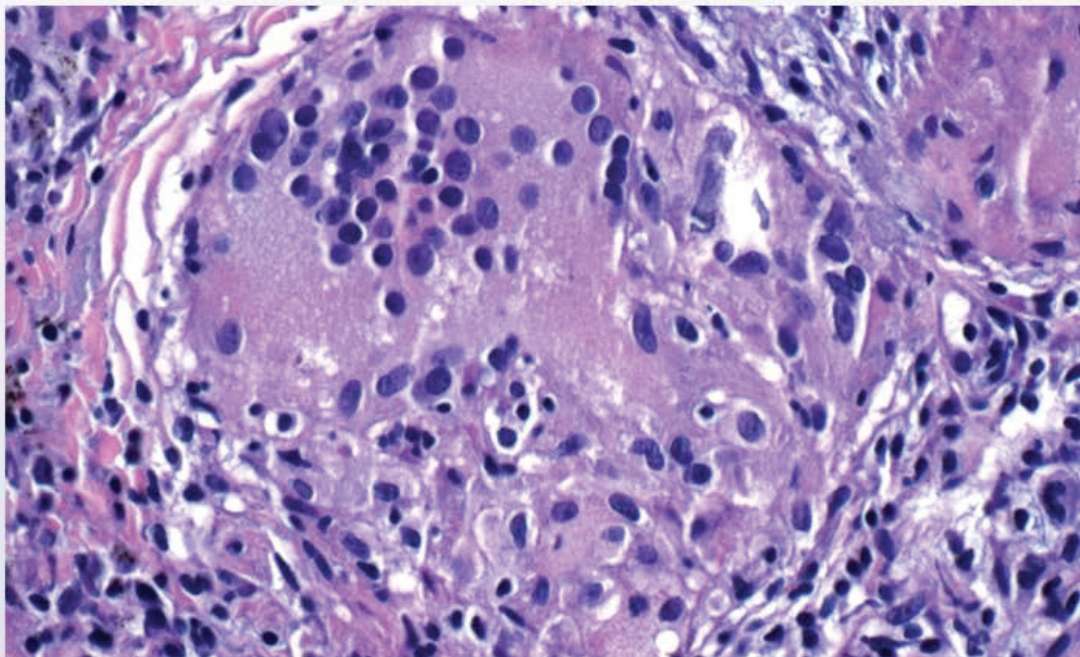


Text Zoom



Settings

A 27-year-old woman undergoes laparotomy for right lower quadrant pain and is found to have an inflamed terminal ileum. The involved segment of the intestine is removed, and the lesion observed on light microscopy is seen in the image.







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

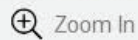
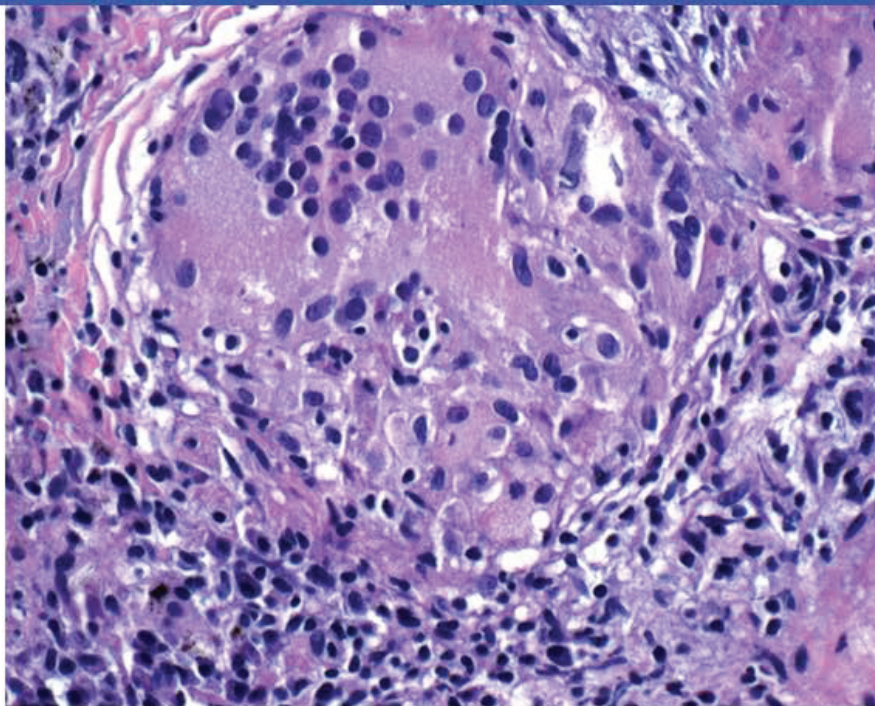


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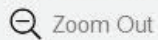


Settings

## Exhibit Display



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook

Block Time Remaining: 00:33:14

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1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

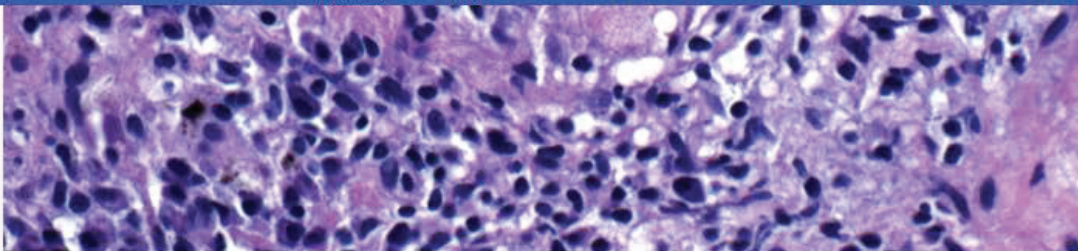
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following cell types most likely mediated the formation of this patient's lesion?

- ☐ A. B-lymphocytes
- ☐ B. Eosinophils
- ☐ C. Neutrophils
- ☐ D. Natural killer cells
- ☐ E. Th1 cells
- ☐ F. Th2 cells

**Submit**

Block Time Remaining: 00:33:18

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



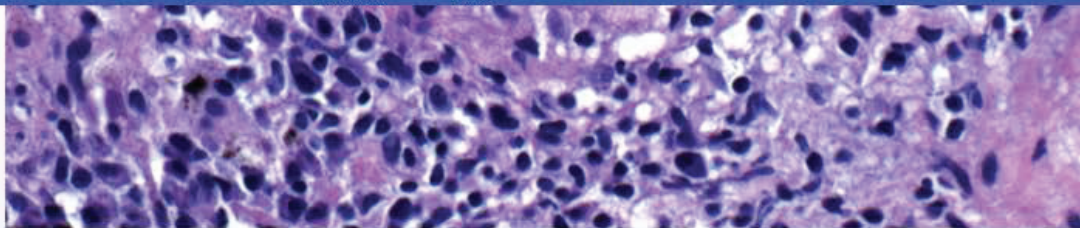
Reverse Color



Text Zoom



Settings



Which of the following cell types most likely mediated the formation of this patient's lesion?

- ☐ A. B-lymphocytes (8%)
- ☐ B. Eosinophils (1%)
- ☐ C. Neutrophils (8%)
- ☐ D. Natural killer cells (0%)
- ☒ E. Th1 cells (71%)
- ☐ F. Th2 cells (10%)

Correct

71%



39 secs



09/16/2020



Feedback

Suspend

End Block

<https://t.me/USMLEWorldStep1>





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



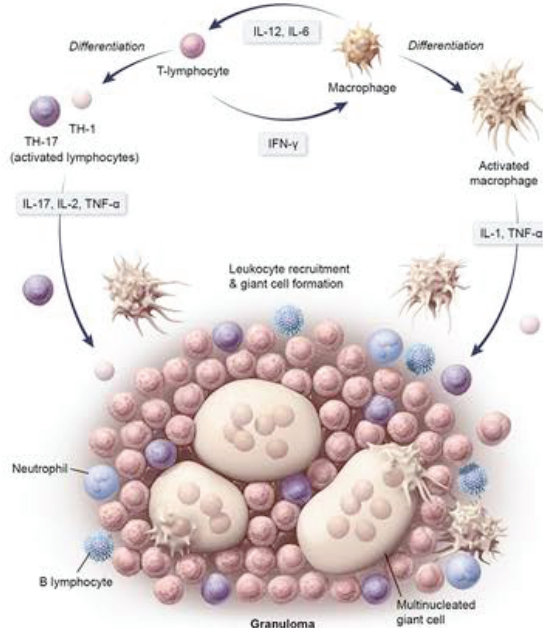
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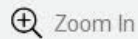
## Exhibit Display

## Pathogenesis of granulomas

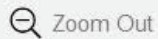


IFN = interferon; TH = T helper; TNF = tumor necrosis factor.

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Reset



New



Existing



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1



Feedback



Suspend



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

IFN = interferon; TH = T helper; TNF = tumor necrosis factor.

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This patient has abdominal pain, ileal inflammation, and a **noncaseating granuloma** on biopsy, all of which are consistent with Crohn disease (CD). Noncaseating granulomas are seen only in a minority of patients with CD but, when present, are highly suggestive of the diagnosis. Microscopically, granulomas contain a large number of epithelioid macrophages that may fuse together to form multinucleated cells (Langhans giant cells), surrounded by a band of lymphocytes.

Granulomas are considered caseating or noncaseating:

- **Caseating:** Central necrosis is present and has a granular, cheesy appearance. Caseating granulomas are typically seen in infectious etiologies (eg, tuberculosis, leprosy, syphilis, cat scratch disease) due to cell death (both macrophage and bacterial) and the release of cellular contents.
- **Noncaseating:** No central necrosis is present. Noncaseating granulomas are typically seen in autoimmune conditions (eg, CD, sarcoidosis, common variable immune deficiency).

Granuloma formation is a product of chronic T-lymphocyte and macrophage activation in response to a difficult-to-eradicate antigen (eg, mycobacterium, self-antigens). Macrophages release tumor necrosis factor- $\alpha$  and other proinflammatory cytokines (eg, IL-6, IL-1, **IL-12**) that promote macrophage migration and **Th1 cell differentiation**. Th1 cells are thought to be important in granuloma organization;





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

autoinflammatory conditions (eg, CD, sarcoidosis, common variable immune deficiency).

Granuloma formation is a product of chronic T-lymphocyte and macrophage activation in response to a difficult-to-eradicate antigen (eg, mycobacterium, self-antigens). Macrophages release tumor necrosis factor- $\alpha$  and other proinflammatory cytokines (eg, IL-6, IL-1, **IL-12**) that promote macrophage migration and **Th1 cell differentiation**. Th1 cells are thought to be important in granuloma organization; they produce IL-2 and **interferon-gamma**, which promote further T-cell response, **activation of macrophages**, and differentiation of macrophages into giant cells. Th17 cells are a proinflammatory subset of Th1 cells and contribute to the cell injury seen in CD.

**(Choice A)** B-lymphocytes differentiate into plasma cells and produce antibodies, thereby mediating the immune response to bacterial infection.

**(Choice B)** Eosinophils mediate defense reactions against certain parasites. They are also implicated in the pathogenesis of hypersensitivity reactions.

**(Choice C)** The main function of neutrophils is phagocytosis. They play an active role in nonspecific inflammatory processes.

**(Choice D)** Natural killer (NK) cells provide a nonspecific defense against virus-infected and tumor cells. They are not known to play a role in CD.



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice B)** Eosinophils mediate defense reactions against certain parasites. They are also implicated in the pathogenesis of hypersensitivity reactions.

**(Choice C)** The main function of neutrophils is phagocytosis. They play an active role in nonspecific inflammatory processes.

**(Choice D)** Natural killer (NK) cells provide a nonspecific defense against virus-infected and tumor cells. They are not known to play a role in CD.

**(Choice F)** Th2 cells are involved in the pathogenesis of ulcerative colitis. They produce IL-5 and IL-13, which contribute to inflammation and damage of the intestinal mucosa.

### Educational objective:

Granulomas are characterized by a large number of epithelioid macrophages that may fuse together to form multinucleated cells (Langhans giant cells) surrounded by a band of lymphocytes. Granuloma formation involves chronic Th1 and macrophage activation in response to a difficult-to-eradicate antigen.

Pathology

Gastrointestinal &amp; Nutrition

Inflammatory bowel disease

Subject

System

Topic

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Block Time Remaining: 00:33:49

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 53-year-old man with nocturnal cough undergoes an upper endoscopy with esophageal biopsy. Light microscopy of the tissue specimen shows elongation of the lamina propria papillae with several eosinophils and neutrophils scattered within the squamous epithelium. The patient takes metformin and enalapril for diabetes mellitus and hypertension, respectively. He is started on pantoprazole, and after 2 weeks his cough symptoms resolve. Which of the following was the most likely cause of his symptoms?

- ☐ A. Absent esophageal peristaltic movements
- ☐ B. Allergen-mediated esophageal disease
- ☐ C. Gastroesophageal junction incompetence
- ☐ D. Mucosal disruption from fungal infection
- ☐ E. Mucosal disruption from viral infection
- ☐ F. Pill-induced esophageal mucosa damage

**Submit**

Block Time Remaining: 00:33:50

<https://t.me/USMLEWorldStep1>

0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 53-year-old man with nocturnal cough undergoes an upper endoscopy with esophageal biopsy. Light microscopy of the tissue specimen shows elongation of the lamina propria papillae with several eosinophils and neutrophils scattered within the squamous epithelium. The patient takes metformin and enalapril for diabetes mellitus and hypertension, respectively. He is started on pantoprazole, and after 2 weeks his cough symptoms resolve. Which of the following was the most likely cause of his symptoms?

- ☐ A. Absent esophageal peristaltic movements (1%)
- ☐ B. Allergen-mediated esophageal disease (18%)
- ☒ C. Gastroesophageal junction incompetence (67%)
- ☐ D. Mucosal disruption from fungal infection (3%)
- ☐ E. Mucosal disruption from viral infection (1%)
- ☐ F. Pill-induced esophageal mucosa damage (8%)

Correct



67%

Answered correctly



58 secs

Time Spent



01/05/2021

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Feedback



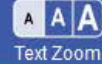
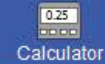
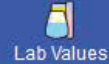
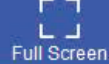
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## Gastroesophageal reflux disease

<b>Pathophysiology</b>	<ul style="list-style-type: none"><li>• Decreased tone or excessive transient relaxation of LES</li><li>• Anatomic disruption to gastroesophageal junction (eg, hiatal hernia)</li><li>• ↑ Risk with obesity, pregnancy, smoking, alcohol intake</li></ul>
<b>Manifestations</b>	<ul style="list-style-type: none"><li>• Regurgitation of acidic material in mouth</li><li>• Heartburn</li><li>• Odynophagia (often indicates reflux esophagitis)</li><li>• Extraesophageal symptoms (eg, cough, laryngitis, wheezing)</li></ul>
<b>Complications</b>	<ul style="list-style-type: none"><li>• Erosive esophagitis</li><li>• Strictures</li><li>• Barrett esophagus → adenocarcinoma</li></ul>
<b>Initial treatment</b>	<ul style="list-style-type: none"><li>• Lifestyle (eg, weight loss) &amp; dietary changes</li><li>• H2R blocker or proton pump inhibitor</li></ul>

**H2R** = histamine 2 receptor; **LES** = lower esophageal sphincter.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**Gastroesophageal reflux disease** (GERD) is a very common condition that usually manifests with heartburn, regurgitation, and dysphagia. However, patients can have **extraesophageal symptoms** (eg, nocturnal **cough**, hoarseness) in the absence of heartburn ("silent GERD").

**Gastroesophageal junction incompetence** is the primary pathophysiologic mechanism responsible for GERD. This incompetence is most commonly caused by excessive relaxation of the lower esophageal sphincter, resulting in the reflux of acidic gastric contents back into the esophagus. Irritation of the esophageal mucosa leads to an inflammatory reaction with mucosal erythema and edema; erosions/ulcerations may develop in severe cases. Characteristic histologic findings include basal zone hyperplasia, elongation of the **lamina propria papillae**, and scattered eosinophils and neutrophils.

**(Choice A)** Absent esophageal peristaltic movements can be seen with achalasia and systemic sclerosis. The distinctive histopathologic findings of systemic sclerosis involving the esophagus include atrophy of the muscularis with collagenous fibrosis.

**(Choice B)** **Eosinophilic esophagitis** is an immune/antigen-mediated disease that typically presents with dysphagia and food impaction in atopic adults. It is characterized histologically by *numerous* superficially located intraepithelial eosinophils, which can help differentiate it from reflux esophagitis.

**(Choice D)** *Candida albicans* is the most common cause of infectious esophagitis in HIV and



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice D)** *Candida albicans* is the most common cause of infectious esophagitis in HIV and immunocompromised patients. Endoscopy typically shows white plaques on an erythematous mucosa, and light microscopy demonstrates **pseudohyphae** and budding spores embedded in necrotic debris.

**(Choice E)** Herpes simplex virus (HSV) and cytomegalovirus (CMV) are other common causes of infectious esophagitis in immunocompromised patients. **HSV** usually shows punched-out ulcers on endoscopy with eosinophilic nuclear inclusions on biopsy. In contrast, **CMV** produces shallow/linear ulcers with nuclear/cytoplasmic viral inclusions.

**(Choice F)** Pill-induced esophagitis is commonly seen with tetracycline antibiotics, potassium chloride, and bisphosphonates. Metformin and enalapril do not cause esophagitis.

### Educational objective:

Gastroesophageal reflux disease is caused primarily by gastroesophageal junction incompetence and can be associated with extraesophageal symptoms (eg, nocturnal cough) in the absence of heartburn ("silent GERD"). Acidic gastric contents irritate the esophageal mucosa, leading to characteristic histologic findings that include basal zone hyperplasia, elongation of the lamina propria papillae, and scattered eosinophils.



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 46-year-old man comes to the emergency department due to severe anal pain. He has a history of chronic constipation and on several occasions has noticed streaks of blood on the tissue paper after wiping. He has no abdominal pain, nausea, vomiting, or weight loss and has no family history of malignancy. His temperature is 36.7 C (98 F). On examination, there are several large, purplish-blue sacs bulging into the anal canal, one of which originates below the dentate line and is extremely tender. Excision of the tender lesion under local anesthesia is planned. The anesthetic agent most likely blocks sensory impulses carried by which of the following structures?

- ☐ A. Ilioinguinal nerve
- ☐ B. Inferior gluteal nerve
- ☐ C. Inferior hypogastric plexus
- ☐ D. Pelvic splanchnic nerves
- ☐ E. Pudendal nerve

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Block Time Remaining: 00:34:48

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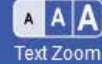
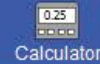
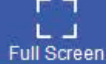
Feedback



Suspend



End Block



A 46-year-old man comes to the emergency department due to severe anal pain. He has a history of chronic constipation and on several occasions has noticed streaks of blood on the tissue paper after wiping. He has no abdominal pain, nausea, vomiting, or weight loss and has no family history of malignancy. His temperature is 36.7 C (98 F). On examination, there are several large, purplish-blue sacs bulging into the anal canal, one of which originates below the dentate line and is extremely tender. Excision of the tender lesion under local anesthesia is planned. The anesthetic agent most likely blocks sensory impulses carried by which of the following structures?

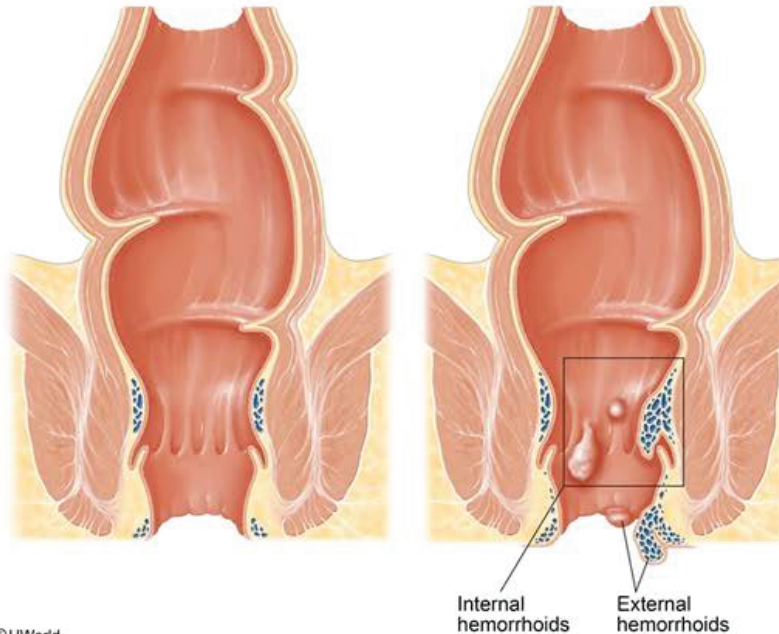
- ☐ A. Ilioinguinal nerve (3%)
- ☐ B. Inferior gluteal nerve (5%)
- ☐ C. Inferior hypogastric plexus (3%)
- ☐ D. Pelvic splanchnic nerves (5%)
- ☒ E. Pudendal nerve (83%)



Exhibit Display

Normal venous plexus

Hemorrhoids



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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internal hemorrhoids

external hemorrhoids

This patient has both internal and **external hemorrhoids**, which each have a distinct epithelial lining and innervation. Internal hemorrhoids originate above the dentate line and are covered by columnar epithelium. They have autonomic innervation from the inferior hypogastric plexus, which is only sensitive to stretch and not pain, temperature, or touch.

External hemorrhoids, which originate below the dentate line, are covered by modified squamous epithelium and have cutaneous (somatic) nervous innervation from the inferior rectal nerve, a branch of the pudendal nerve. **Branches** of the **pudendal nerve** supply the perineum and external genitalia in males and females and are very sensitive to touch, temperature, and **pain**. External hemorrhoids are generally asymptomatic but can become exquisitely painful if they thrombose, as in this case.

**(Choice A)** The ilioinguinal nerve is mostly sensory, derived from L1, and carries sensation from skin of the upper and medial part of the thigh, the root of the penis and upper part of the scrotum in males, and the mons pubis and labia majora in females.

**(Choice B)** The inferior gluteal nerve, composed of branches of L5, S1, and S2, is the main nerve supplying motor functions to the gluteus maximus muscle.

**(Choice C)** The inferior hypogastric plexus, which has both sympathetic and parasympathetic



Feedback



Suspend



End Block



the upper and medial part of the thigh, the root of the penis and upper part of the scrotum in males, and the mons pubis and labia majora in females.

**(Choice B)** The inferior gluteal nerve, composed of branches of L5, S1, and S2, is the main nerve supplying motor functions to the gluteus maximus muscle.

**(Choice C)** The inferior hypogastric plexus, which has both sympathetic and parasympathetic components, innervates the internal pelvic viscera but not the external perirectal area.

**(Choice D)** The pelvic splanchnic nerves are derived from S2, S3, and S4 and provide parasympathetic innervation to the pelvic and genital organs.

### Educational objective:

External hemorrhoids, which originate below the dentate line, are covered by modified squamous epithelium and have cutaneous (somatic) nervous innervation from the inferior rectal nerve, a branch of the pudendal nerve.

### References

- [Hemorrhoids.](#)
- [Hemorrhoids.](#)





A 62-year-old man comes to the office for evaluation of abdominal swelling. Over the last few weeks his abdomen has become more distended with associated mild discomfort and decreased appetite. Past medical history includes multiple admissions for alcohol-induced pancreatitis. The patient currently drinks 1 pint of liquor daily and does not use tobacco or illicit drugs. Physical examination reveals mildly icteric sclera and multiple spider angiomas on the upper chest. The abdomen is distended and there is dullness to percussion that changes location when the patient lays on either side. Serum sodium is 130 mEq/dL and creatinine is 1.1 mg/dL. Which of the following would most likely be seen in this patient?

	Serum antidiuretic hormone	Urine sodium	Total body volume
<input type="radio"/> A.	↑	↓	↑
<input type="radio"/> B.	↑	↓	↓
<input type="radio"/> C.	↑	↑	normal
<input type="radio"/> D.	↓	↑	normal







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

abdomen has become more distended with associated mild discomfort and decreased appetite. Past medical history includes multiple admissions for alcohol-induced pancreatitis. The patient currently drinks 1 pint of liquor daily and does not use tobacco or illicit drugs. Physical examination reveals mildly icteric sclera and multiple spider angiomas on the upper chest. The abdomen is distended and there is dullness to percussion that changes location when the patient lays on either side. Serum sodium is 130 mEq/dL and creatinine is 1.1 mg/dL. Which of the following would most likely be seen in this patient?

- |                          | Serum<br>antidiuretic<br>hormone | Urine<br>sodium | Total body<br>volume |
|--------------------------|----------------------------------|-----------------|----------------------|
| <input type="radio"/> A. | ↑                                | ↓               | ↑                    |
| <input type="radio"/> B. | ↑                                | ↓               | ↓                    |
| <input type="radio"/> C. | ↑                                | ↑               | normal               |
| <input type="radio"/> D. | ↓                                | ↑               | normal               |
| <input type="radio"/> E. | ↑                                | ↑               | ↓                    |





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

pint of liquor daily and does not use tobacco or illicit drugs. Physical examination reveals mildly icteric sclera and multiple spider angiomas on the upper chest. The abdomen is distended and there is dullness to percussion that changes location when the patient lays on either side. Serum sodium is 130 mEq/dL and creatinine is 1.1 mg/dL. Which of the following would most likely be seen in this patient?

	Serum antidiuretic hormone	Urine sodium	Total body volume	
<input checked="" type="radio"/> A.	↑	↓	↑	(62%)
<input type="radio"/> B.	↑	↓	↓	(3%)
<input type="radio"/> C.	↑	↑	normal	(20%)
<input type="radio"/> D.	↓	↑	normal	(8%)
<input type="radio"/> E.	↑	↑	↓	(4%)

Correct

62%

02 mins

09/28/2020

Block Time Remaining: 00:36:58

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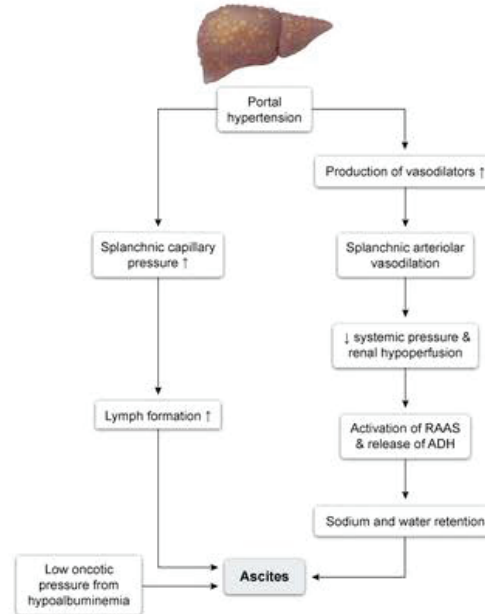
Feedback

Suspend

End Block

### Exhibit Display

#### Pathogenesis of ascites in cirrhosis



ADH = antidiuretic hormone; RAAS = renin-angiotensin-aldosterone system.

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Zoom In Zoom Out Reset New Existing My Notebook





ADH = antidiuretic hormone; RAAS = renin-angiotensin-aldosterone system.

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This patient with a history of heavy alcohol use, abdominal swelling with shifting dullness to percussion (indicative of intraabdominal fluid), and stigmata of chronic liver disease (eg, spider angiomas, jaundice) has **ascites** due to cirrhosis. **Cirrhosis** occurs from progressive hepatic fibrosis, resulting **portal hypertension** due to increased sinusoidal blood flow resistance. There is also increased formation of vasodilatory factors (eg, nitric oxide), possibly due to bacterial products (eg, endotoxins) that accumulate because of reduced host defenses and increased portosystemic shunting. This results in the following hemodynamic alterations:

- Reduced systemic vascular resistance along with blood pooling in the splanchnic vascular bed leads to reduced blood pressure. Heart rate and cardiac output increase to compensate (hyperdynamic circulation).
- Reduced renal perfusion leads to activation of the **renin-angiotensin-aldosterone system (RAAS)** and **increased release of antidiuretic hormone (ADH)** in an effort to restore circulating volume.
- The combined aldosterone and ADH effects lead to **increased renal resorption of sodium** (ie, lower urine sodium) and water.

Although this restores renal perfusion, the resistance to splanchnic flow and hyperdynamic circulation





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Although this restores renal perfusion, the resistance to splanchnic flow and hyperdynamic circulation promotes third-spacing of fluids into the abdominal cavity (ie, ascites) and interstitium (ie, edema). This is compounded by low serum oncotic pressure due to hypoalbuminemia from liver synthetic dysfunction. Therefore, despite **increased total body volume**, patients with cirrhosis remain intravascularly depleted and continue to release hypovolemic hormones. Eventually, the resultant elevated ADH secretion can lead to **hypervolemic hyponatremia**, which is common in patients with advanced cirrhosis.

**(Choices B, C, D, and E)** Splanchnic vasodilation results in renal hypoperfusion, stimulating increased ADH secretion and activation of the RAAS. This leads to increased renal resorption of sodium, lowering the urinary sodium concentration. Third-spacing of fluid results in increased total body volume.

### Educational objective:

Portal hypertension in cirrhosis leads to vasodilation and decreased systemic perfusion pressure, which causes antidiuretic hormone release and activation of the renin-angiotensin-aldosterone system, promoting sodium and water retention. However, due to resistance to splanchnic flow, low oncotic pressure, and hyperdynamic circulation, the fluid is third-spaced into the extravascular compartments (eg, ascites). Therefore, despite increased total body volume, patients with cirrhosis remain intravascularly volume depleted.



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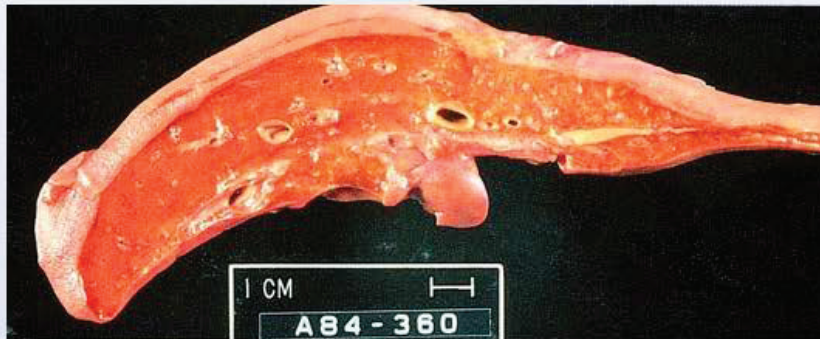
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End Block



A 55-year-old woman comes to the emergency department with nausea, fever, fatigue, and anorexia. She returned a week ago from a trip to Mexico, where she underwent an emergency cholecystectomy without complications. Her temperature is 38.3 C (101 F), blood pressure is 100/60 mm Hg, pulse is 90/min, and respirations are 12/min. The patient is alert and answers questions but appears extremely weak and slightly icteric. She has no other medical problems and takes no medications. She does not use tobacco, alcohol, or illicit drugs. The patient is admitted to the hospital, but her condition worsens and she dies 2 days later. Postmortem viral serologies are negative. Gross examination of the liver on autopsy is shown in the image below.



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Which of the following additional findings would have most likely been found in this patient?

- ☐ A. Decreased serum albumin level
- ☐ B. Distended abdominal veins and ascites
- ☐ C. Normal alanine aminotransferase level
- ☐ D. Palmar erythema
- ☐ E. Prolonged prothrombin time
- ☐ F. Splenomegaly





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Which of the following additional findings would have most likely been found in this patient?

- ☐ A. Decreased serum albumin level (17%)
- ☐ B. Distended abdominal veins and ascites (15%)
- ☐ C. Normal alanine aminotransferase level (15%)
- ☐ D. Palmar erythema (6%)
- ☒ E. Prolonged prothrombin time (32%)
- ☐ F. Splenomegaly (12%)

Correct

32%  
Answered correctly

51 secs  
Time spent

12/19/2020  
Last updated

Block Time Remaining: 00:00:51

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Feedback



Suspend



End Block



This patient presents after a recent surgery with signs and symptoms consistent with **drug-induced liver injury**, most likely due to inhaled anesthetic use. **Inhaled anesthetic hepatotoxicity** is most frequently associated with halothane, which remains one of the most commonly used inhaled anesthetics worldwide. In the United States, halothane has been largely replaced with other halogenated anesthetics, such as enflurane, isoflurane, desflurane, and sevoflurane. Although these agents are safer than halothane, there have been reports of associated hepatotoxicity.

Halogenated inhaled anesthetics predominantly cause a **hepatocellular pattern** of liver injury. This can range from mild asymptomatic aminotransferase elevation to **fulminant hepatitis** with a 50% fatality rate. In severe cases, extensive hepatocellular damage causes the liver to rapidly atrophy and appear **shrunken** on autopsy. Histologically, widespread centrilobular necrosis and inflammation of the portal tracts and parenchyma are observed, making the condition indistinguishable from fulminant viral hepatitis. The underlying mechanism is thought to be a hypersensitivity reaction to the drug that causes an immune-mediated attack against hepatocytes.

Patients suffering from inhaled-anesthetic hepatotoxicity typically have fever, anorexia, nausea, myalgias, arthralgias, and rash. Tender hepatomegaly (reflecting widespread liver inflammation) and jaundice can be present on physical examination. Laboratory findings typically include markedly **elevated serum**







present on physical examination. Laboratory findings typically include markedly **elevated serum**

**aminotransferase levels, prolonged prothrombin time**, leukocytosis, and eosinophilia. The prolonged prothrombin time is due to failure of hepatic synthetic function and deficiency of factor VII (which has the shortest half-life of all the procoagulant factors).

**(Choice A)** Decreased serum albumin levels are commonly seen in patients with chronic, end-stage liver disease as the remaining hepatocytes have reduced functionality. However, acute liver injury presents with normal albumin levels due to the long half-life of albumin (~20 days).

**(Choices B and D)** Distended abdominal veins with ascites and palmar erythema are usually seen in patients with end-stage liver disease (eg, cirrhosis). These findings are not associated with acute hepatic failure.

**(Choice C)** A markedly elevated alanine aminotransferase level would be expected with fulminant hepatic failure.

**(Choice F)** Splenomegaly develops secondary to portal hypertension and can be seen in cirrhotic patients. It is not associated with acute hepatitis.

### **Educational objective:**

Inhaled anesthetics, such as halothane, can be associated with a highly lethal fulminant hepatitis that





normal albumin levels due to the long half-life of albumin (~20 days).

**(Choices B and D)** Distended abdominal veins with ascites and palmar erythema are usually seen in patients with end-stage liver disease (eg, cirrhosis). These findings are not associated with acute hepatic failure.

**(Choice C)** A markedly elevated alanine aminotransferase level would be expected with fulminant hepatic failure.

**(Choice F)** Splenomegaly develops secondary to portal hypertension and can be seen in cirrhotic patients. It is not associated with acute hepatitis.

### Educational objective:

Inhaled anesthetics, such as halothane, can be associated with a highly lethal fulminant hepatitis that cannot be distinguished histologically from acute viral hepatitis. Patients have significantly elevated aminotransferase levels due to massive hepatocellular injury and a prolonged prothrombin time due to failure of hepatic synthetic function.

### References

- [Halothane-induced hepatitis: a forgotten issue in developing countries.](#)





A 54-year-old man with a history of cirrhosis is brought to the emergency department by his wife, who found him agitated and confused. She reports that he was nauseous and vomited bright red blood several times yesterday. His cirrhosis is secondary to chronic hepatitis C infection, and he has received treatment for esophageal varices in the past. Physical examination reveals abdominal distension, decreased liver span, and testicular atrophy. A jerky, irregular flexion-extension tremor involving his hands is seen with wrist extension. Which of the following is most likely to be elevated in this patient's astrocytes?

- ☐ A.  $\alpha$ -ketoglutarate
- ☐ B. Alanine
- ☐ C. Aspartate
- ☐ D. Carbamoyl phosphate
- ☐ E. Glutamine

**Submit**





A 54-year-old man with a history of cirrhosis is brought to the emergency department by his wife, who found him agitated and confused. She reports that he was nauseous and vomited bright red blood several times yesterday. His cirrhosis is secondary to chronic hepatitis C infection, and he has received treatment for esophageal varices in the past. Physical examination reveals abdominal distension, decreased liver span, and testicular atrophy. A jerky, irregular flexion-extension tremor involving his hands is seen with wrist extension. Which of the following is most likely to be elevated in this patient's astrocytes?

- ☐ A.  $\alpha$ -ketoglutarate (17%)
- ☐ B. Alanine (13%)
- ☐ C. Aspartate (10%)
- ☐ D. Carbamoyl phosphate (14%)
- ☒ E. Glutamine (44%)

Correct



44%

Answered correctly



49 secs

Time Spent



10/18/2020

Last Updated

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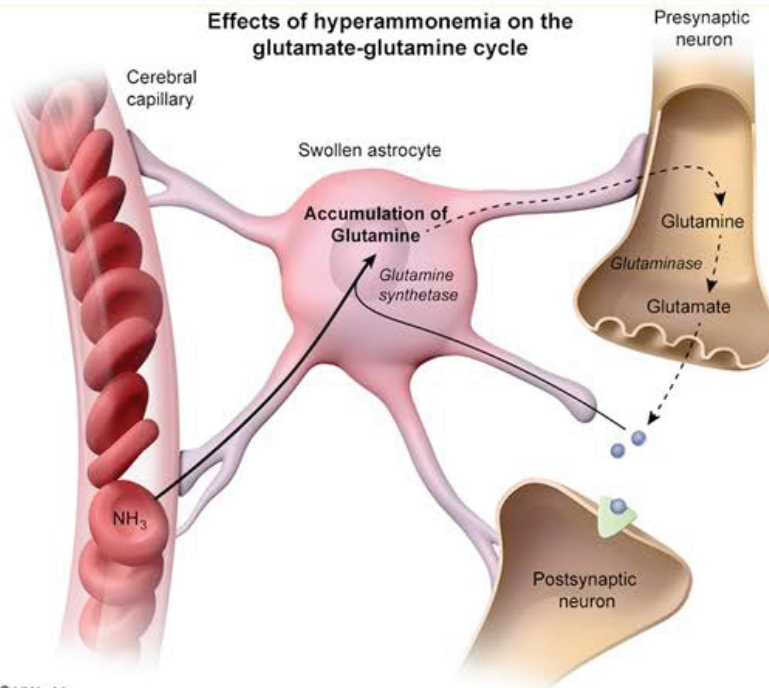
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## Exhibit Display

## Effects of hyperammonemia on the glutamate-glutamine cycle



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This patient has **hepatic encephalopathy**, likely due to his recent gastrointestinal bleeding causing a corresponding increase in nitrogen absorption by the gut. The pathogenesis of hepatic encephalopathy is related to increased circulatory levels of **ammonia** and other neurotoxins due to failure of the liver to metabolize waste products.

Under normal conditions, astrocytes regulate neurotransmission by taking up glutamate present in the synapse, preventing excessive neuronal excitation. Through the action of glutamine synthetase, glutamate undergoes a condensation reaction with ammonia to form glutamine (a non-neuroactive compound). Glutamine is then released by the astrocytes and taken up by neurons, where it is converted back to glutamate for use as a neurotransmitter (**glutamate-glutamine cycle**).

When **excess ammonia** is present in the blood, it crosses the blood-brain barrier and is taken up by astrocytes, **increasing glutamine production**. The presence of excess glutamine within astrocytes leads to increased intracellular osmolarity, causing astrocyte swelling and impaired glutamine release. Hyperammonemia consequently decreases the amount of glutamine available for conversion to glutamate in neurons, resulting in **disruption of excitatory neurotransmission**.

**(Choice A)**  $\alpha$ -ketoglutarate functions as a key intermediate in the TCA cycle and as a nitrogen transporter





Exhibit Display

Hepatic encephalopathy

Precipitating factors

- Drugs (eg, sedatives, narcotics)
- Hypovolemia (eg, diarrhea)
- Electrolyte changes (eg, hypokalemia)
- ↑ Nitrogen load (eg, GI bleeding)
- Infection (eg, pneumonia, UTI, SBP)
- Portosystemic shunting (eg, TIPS)

Clinical presentation

- Sleep pattern changes
- Altered mental status
- Ataxia
- Asterixis

Treatment

- Correct precipitating causes (eg, fluids, antibiotics)
- ↓ Blood ammonia concentration (eg, lactulose, rifaximin)

GI = gastrointestinal; SBP = spontaneous bacterial peritonitis; TIPS = transjugular intrahepatic portosystemic shunt; UTI = urinary tract infection.

This patient has hepatic encephalopathy, a condition corresponding increase in ammonia levels related to increased metabolism waste products.

Under normal conditions, the blood-brain synapse, preventing ammonia from entering the brain. Undergoes a condensation reaction. Glutamine is then released into the brain. Glutamate for use as a neurotransmitter.

When excess ammonia enters the brain, astrocytes, increase their production of glutamine to increased intracellular levels. Hyperammonemia leads to increased ammonia in neurons, resulting in neuronal damage.

(Choice A) α-keto

⚡ New | Existing



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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**(Choice A)**  $\alpha$ -ketoglutarate functions as a key intermediate in the TCA cycle and as a nitrogen transporter

in metabolic reactions. In the setting of hyperammonemia, ammonia is detoxified to glutamate via glutamate dehydrogenase, depleting  $\alpha$ -ketoglutarate and impairing energy metabolism in the brain.

**(Choice B)** Alanine is an amino group transporter in the [glucose-alanine cycle](#) in liver and muscle tissue.

This process allows tissues that use amino acids for fuel to shunt excess nitrogen back to the liver.

**(Choice C)** Aspartate is a nonessential amino acid that functions as a substrate in the urea cycle and as part of the malate-aspartate shuttle that transfers cytosolic-reducing equivalents into the mitochondrial matrix.

**(Choice D)** Carbamoyl phosphate is a urea cycle intermediate synthesized by carbamoyl phosphate synthetase I, which transfers an ammonia molecule from glutamine or glutamate to a phosphorylated bicarbonate. Carbamoyl phosphate production is decreased in patients with advanced liver disease.

### Educational objective:

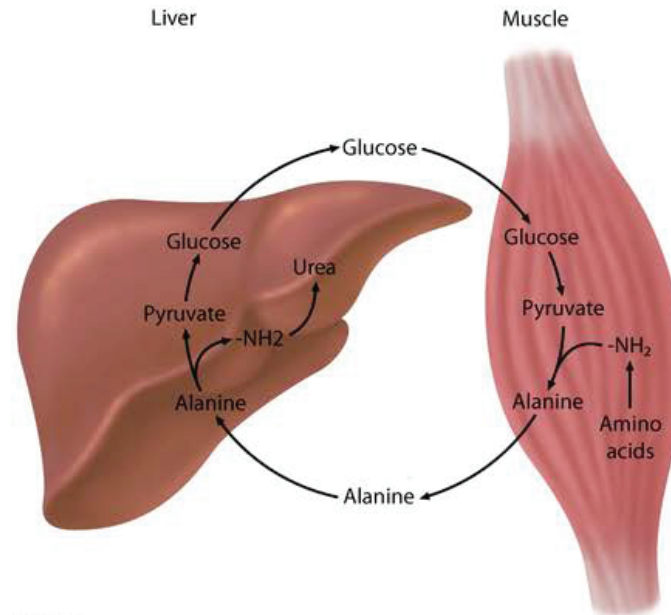
Hyperammonemia in advanced liver failure occurs as a direct result of the cirrhotic liver's inability to metabolize nitrogenous waste products. Ammonia crosses the blood-brain barrier and causes excess glutamine to accumulate within astrocytes. This decreases the amount of glutamine available for conversion to glutamate in the neurons, resulting in disruption of excitatory neurotransmission.



(Choice A)  $\alpha$ -ketoglutarate functions as a key intermediate in the TCA cycle and as a nitrogen transporter

## Exhibit Display

## Glucose-alanine cycle







Biochemistry researchers are investigating the speed at which various carbohydrates are metabolized within the liver. They hypothesize that different monosaccharides delivered to the liver have different rates of intracellular metabolism. Which of the following substances is most likely to have the fastest rate of metabolism in the glycolytic pathway?

- ☐ A. Fructose-1-phosphate
- ☐ B. Galactose-1-phosphate
- ☐ C. Glucose-1-phosphate
- ☐ D. Glucose-6-phosphate
- ☐ E. Mannose-6-phosphate

Submit






Biochemistry researchers are investigating the speed at which various carbohydrates are metabolized within the liver. They hypothesize that different monosaccharides delivered to the liver have different rates of intracellular metabolism. Which of the following substances is most likely to have the fastest rate of metabolism in the glycolytic pathway?

- ☒ A. Fructose-1-phosphate (39%)
- ☐ B. Galactose-1-phosphate (1%)
- ☐ C. Glucose-1-phosphate (11%)
- ☐ D. Glucose-6-phosphate (45%)
- ☐ E. Mannose-6-phosphate (1%)

Correct

 39%  
Answered correctly

 11 secs  
Time Spent

 12/11/2020  
Last Updated

Explanation

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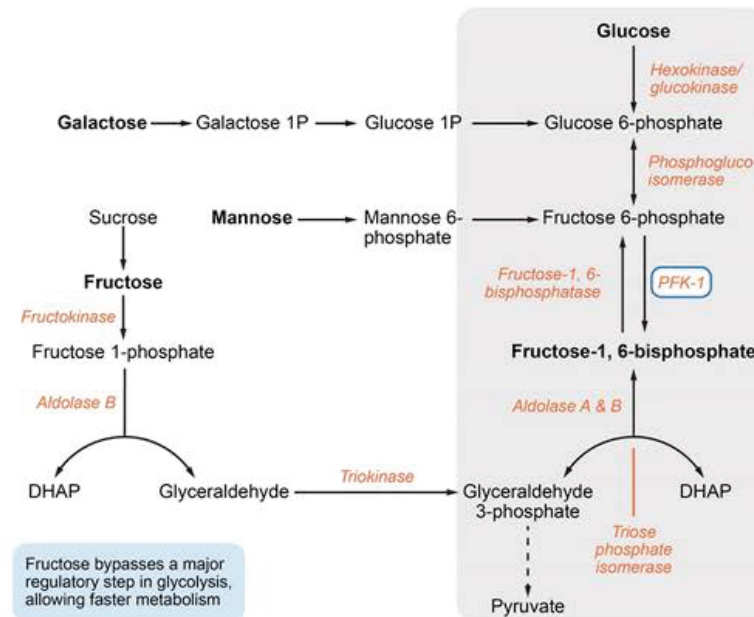


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## Exhibit Display

## Non-glucose monosaccharides &amp; glycolysis



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allowing faster metabolism

Pyruvate

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**Non-glucose monosaccharides** (eg, galactose, mannose, fructose) enter the glycolytic pathway at different points as **intermediates of glycolysis**. Of these, **fructose** is the only one whose metabolites **bypass phosphofructokinase**, one of the key enzymes involved in regulating the rate of glycolysis. As a result, fructose is metabolized by the liver faster than the other monosaccharides and is rapidly cleared from the bloodstream following dietary absorption.

Metabolism of fructose in the liver begins with phosphorylation by fructokinase to **fructose-1-phosphate (F1P)**. Aldolase B can use both fructose-1,6-bisphosphate and F1P as substrates; it converts F1P into **dihydroxy acetone phosphate (DHAP)** and **glyceraldehyde**. Glyceraldehyde can be either phosphorylated to glyceraldehyde-3-phosphate by triokinase or converted to DHAP. DHAP is converted by triose phosphate isomerase to glyceraldehyde-3-phosphate, which continues down the glycolytic pathway.

**(Choices B, C, D, and E)** Galactose-1-phosphate, glucose-1-phosphate, glucose-6-phosphate, and mannose-6-phosphate enter glycolysis upstream of phosphofructokinase, a major rate-limiting enzyme of glycolysis. This slows down the rate of their metabolism relative to fructose and its metabolites (eg, F1P).

**Educational objective:**

Dietary fructose is absorbed in the liver to F1P and is rapidly metabolized because it bypasses



from the bloodstream following dietary absorption.

Metabolism of fructose in the liver begins with phosphorylation by fructokinase to **fructose-1-phosphate (F1P)**. Aldolase B can use both fructose-1,6-bisphosphate and F1P as substrates; it converts F1P into **dihydroxy acetone phosphate (DHAP)** and **glyceraldehyde**. Glyceraldehyde can be either phosphorylated to glyceraldehyde-3-phosphate by triokinase or converted to DHAP. DHAP is converted by triose phosphate isomerase to glyceraldehyde-3-phosphate, which continues down the glycolytic pathway.

**(Choices B, C, D, and E)** Galactose-1-phosphate, glucose-1-phosphate, glucose-6-phosphate, and mannose-6-phosphate enter glycolysis upstream of phosphofructokinase, a major rate-limiting enzyme of glycolysis. This slows down the rate of their metabolism relative to fructose and its metabolites (eg, F1P).

### Educational objective:

Dietary fructose is phosphorylated in the liver to F1P and is rapidly metabolized because it bypasses PFK-1, the major rate-limiting enzyme of glycolysis. Other sugars (eg, glucose, galactose, mannose) enter glycolysis prior to PFK-1 and as a result are metabolized more slowly.

Biochemistry

Gastrointestinal & Nutrition

Glycolysis

Subject

System

Topic

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A 23-year-old man comes to the physician due to a 2-month history of fatigue, malaise, and abdominal discomfort. He is found to have tender hepatomegaly with elevated liver function tests. The patient has never been vaccinated against hepatitis. He has had no raw or uncooked foods recently and recalls no ill contacts. There is no history of blood transfusion. The patient is a graduate student who immigrated to the United States 2 years ago and has not traveled outside the country since. He smokes 2 packs of cigarettes a day and consumes 1 or 2 bottles of beer on weekends. The patient does not use illicit drugs. He has had several episodes of unprotected sex with different female partners within the past year. Which of the following is most likely to be present in this patient?

- ☐ A. HAV in the stool
- ☐ B. Serum anti-HAV IgM
- ☐ C. Serum anti-HBsAg IgG
- ☒ D. Serum HBsAg
- ☐ E. Hepatitis C virus RNA viral load in blood
- ☐ F. Serum anti-hepatitis D virus IgG







never been vaccinated against hepatitis. He has had no raw or uncooked foods recently and recalls no ill contacts. There is no history of blood transfusion. The patient is a graduate student who immigrated to the United States 2 years ago and has not traveled outside the country since. He smokes 2 packs of cigarettes a day and consumes 1 or 2 bottles of beer on weekends. The patient does not use illicit drugs. He has had several episodes of unprotected sex with different female partners within the past year. Which of the following is most likely to be present in this patient?

- ☐ A. HAV in the stool (0%)
- ☐ B. Serum anti-HAV IgM (1%)
- ☐ C. Serum anti-HBsAg IgG (7%)
- ☒ D. Serum HBsAg (79%)
- ☐ E. Hepatitis C virus RNA viral load in blood (10%)
- ☐ F. Serum anti-hepatitis D virus IgG (0%)

Correct

79%



01 min, 31 secs



09/28/2020

Block Time Remaining: 00:03:22

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Feedback



Suspend



End Block



The main modes of transmission of **hepatitis B virus (HBV)** are sexual (transmission among heterosexual partners and among men who have sex with men) and percutaneous (eg, intravenous drug use, needlestick accidents, blood transfusions). Vertical (mother-to-child) transmission is common in high-prevalence areas. This **unvaccinated** patient with tender hepatomegaly and liver function abnormalities most likely has acute HBV infection contracted during an episode of **unprotected sex** (most common mode of transmission in developed countries, >70% of cases). Serum hepatitis B surface antigen (HBsAg) would be present.

Anti-HBsAg immunoglobulin G (IgG) appears after either successful HBV vaccination or HBsAg clearance and remains detectable for life (indicator of non-infectivity and immunity). Because this patient is symptomatic, he obviously has not cleared the virus and would likely not yet have anti-HBsAg IgG (**Choice C**).

**(Choices A and B)** Hepatitis A virus (HAV) in the stool or serum anti-HAV IgM would be expected with acute HAV following recent travel to an endemic area or consumption of tainted, insufficiently heated food (eg, oysters). HAV (fecal-oral transmission) is not usually symptomatic for 2 months and is not associated with a chronic carrier state.

**(Choice E)** Hepatitis C virus (HCV) infection is most often asymptomatic. Also, most HCV transmission





**(Choice E)** Hepatitis C virus (HCV) infection is most often asymptomatic. Also, most HCV transmission occurs in the setting of intravenous drug use. Sexual transmission of HCV can occur but is inefficient; the risk is actually low (eg, incidence of 0.07% per year in a study of 500 heterosexual couples) and would be lower than that of HBV transmission.

**(Choice F)** Hepatitis D virus (HDV) transmission occurs primarily through inoculations and blood transfusions, with sexual transmission far less common. Co-infection with HBV or superinfection of chronic HBV is necessary. Globally, only about 5% of HBV carriers also have HDV (rates vary based on geography).

### Educational objective:

The main modes of transmission of hepatitis B virus include sexual (among both heterosexual partners and men who have sex with men) and percutaneous (eg, intravenous drug use, needlestick accidents, blood transfusions). The risk of sexual transmission of hepatitis C virus is low.

Microbiology

Subject

Gastrointestinal &amp; Nutrition

System

Hepatitis b

Topic

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A 14-year-old Caucasian boy is brought to the physician by his mother due to chronic diarrhea and failure to gain weight appropriately. He has a history of recurrent respiratory infections, and prior sputum cultures have been positive for *Pseudomonas aeruginosa*. His younger brother died from a severe respiratory infection at age 9. Which of the following agents is most likely to improve this patient's condition in the long term?

- ☐ A. Antimotility agents
- ☐ B. Gluten-free diet
- ☐ C. Metronidazole
- ☐ D. Octreotide
- ☐ E. Pancreatic lipase
- ☐ F. Sulfasalazine

**Submit**



A 14-year-old Caucasian boy is brought to the physician by his mother due to chronic diarrhea and failure to gain weight appropriately. He has a history of recurrent respiratory infections, and prior sputum cultures have been positive for *Pseudomonas aeruginosa*. His younger brother died from a severe respiratory infection at age 9. Which of the following agents is most likely to improve this patient's condition in the long term?

- ☐ A. Antimotility agents (2%)
- ☐ B. Gluten-free diet (6%)
- ☐ C. Metronidazole (5%)
- ☐ D. Octreotide (5%)
- ☒ E. Pancreatic lipase (71%)
- ☐ F. Sulfasalazine (8%)

Correct



71%

Answered correctly



27 secs

Time Spent



01/20/2021

Last Updated

Block Time Remaining: 00:03:49

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Feedback



Suspend



End Block



## Features of cystic fibrosis

### Pathogenesis

- Autosomal recessive mutation ( $\Delta F508$ ) impairs CFTR function
- Decreased water content causes **thick, viscous mucus**:
  - Chronic airway obstruction
  - Gastrointestinal malabsorption

### Clinical manifestations

- Chronic, productive cough
- Recurrent **sinopulmonary infections** (eg, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, & *Burkholderia cepacia* complex)
- **Pancreatic insufficiency**
- Male infertility (bilateral absence of vas deferens)





**Diagnosis**

- Elevated sweat chloride levels
- Nasal potential difference measurements
- Genetic testing for *CFTR* mutations

**CFTR** = cystic fibrosis transmembrane conductance regulator.

This young Caucasian patient has a history of recurrent respiratory infections caused by *Pseudomonas aeruginosa*, chronic diarrhea, and failure to thrive. These findings, along with a family history of early sibling death from pulmonary infection, suggest a diagnosis of cystic fibrosis. Steatorrhea and failure to thrive occur as a result of malabsorption due to obstructive fibrosis and progressive insufficiency of the exocrine pancreas. Pancreatic lipase supplementation is likely to improve this patient's condition by enhancing macronutrient and vitamin absorption.

**(Choice A)** Agents that decrease gastrointestinal motility (eg, opiates such as loperamide) can help decrease the volume of diarrhea by slowing intestinal transit time and allowing greater net fluid resorption. However, antimotility agents would not improve the deficiencies in nutrient absorption.

**(Choice B)** A gluten-free diet is the mainstay of treatment for celiac sprue but would be unlikely to help this patient's malabsorption.





patient's malabsorption.

**(Choice C)** Metronidazole is effective only for diarrhea due to infectious causes (eg, giardiasis). This patient's diarrhea is more likely due to malabsorption secondary to cystic fibrosis.

**(Choice D)** Octreotide is a somatostatin analogue that decreases gut motility, blood flow, and endocrine and exocrine pancreatic function. Octreotide decreases secretion of pancreatic enzymes into the intestine and could therefore aggravate this patient's malabsorptive diarrhea and associated nutritional deficiencies.

**(Choice F)** 5-aminosalicylates (eg, sulfasalazine, mesalamine) are used to treat inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. They work by inhibiting cytokine, prostaglandin, and leukotriene synthesis during inflammation. This patient's diarrhea and weight loss are not caused by inflammation.

### Educational objective:

In a young Caucasian patient, the combination of recurrent respiratory infections with *Pseudomonas aeruginosa*, diarrhea, and failure to thrive suggests a diagnosis of cystic fibrosis. Cystic fibrosis causes steatorrhea and failure to thrive due to malabsorption secondary to pancreatic insufficiency, which can be corrected by pancreatic enzyme supplementation.





A 20-year-old man is evaluated in the clinic due to intermittent episodes of self-resolving jaundice. His symptoms are not provoked by any particular circumstances or events. The patient otherwise feels healthy and has no other symptoms. He does not use tobacco, alcohol, or illicit drugs. Complete blood count is within normal limits. Liver function studies are as follows:

Total protein	6.5 g/dL
Albumin	4 g/dL
Total bilirubin	2.8 mg/dL
Direct bilirubin	2.0 mg/dL
Alkaline phosphatase	90 U/L
Aspartate aminotransferase	28 U/L
Alanine	30 U/L







Alkaline phosphatase 90 U/L

Aspartate  
aminotransferase 28 U/L

Alanine  
aminotransferase 30 U/L

Liver biopsy shows abundant pigment inclusions in the lysosomes of the otherwise normal hepatocytes. Electron spin resonance spectroscopy reveals that the pigment is composed of polymers of epinephrine metabolites. Which of the following is the most likely cause of this patient's jaundice?

- ☐ A. Defective hepatocellular excretion of bilirubin glucuronides
- ☐ B. Impaired conjugation of bilirubin
- ☐ C. Increased production of catecholamines
- ☐ D. Ineffective intramedullary erythropoiesis
- ☐ E. Low serum ceruloplasmin





aminotransferase

20 U/L

Alanine

30 U/L

aminotransferase

Liver biopsy shows abundant pigment inclusions in the lysosomes of the otherwise normal hepatocytes. Electron spin resonance spectroscopy reveals that the pigment is composed of polymers of epinephrine metabolites. Which of the following is the most likely cause of this patient's jaundice?

- ☒ A. Defective hepatocellular excretion of bilirubin glucuronides (61%)
- ☐ B. Impaired conjugation of bilirubin (13%)
- ☐ C. Increased production of catecholamines (17%)
- ☐ D. Ineffective intramedullary erythropoiesis (1%)
- ☐ E. Low serum ceruloplasmin (4%)

Correct



61%

Answered correctly



01 min, 40 secs

Time spent



02/14/2021

Last updated

Block Time Remaining: 00:05:29

TUTOR

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block



Item 6 of 40

Question Id: 101



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



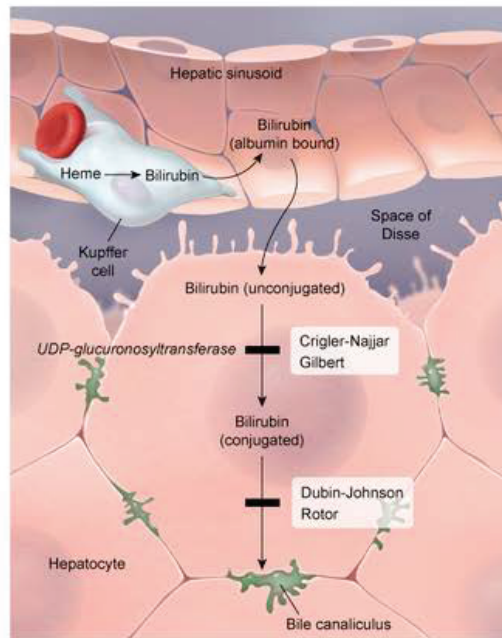
Text Zoom



Settings

## Exhibit Display

## Bilirubin metabolism



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Zoom In

Zoom Out

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New | Existing

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Dubin-Johnson

Block Time Remaining: 00:05:29

TUTOR

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block





**Dubin-Johnson syndrome** is a benign autosomal recessive disorder characterized by defective hepatic excretion of bilirubin glucuronides due to a mutation in the canalicular membrane transport protein.

Individuals with this condition can develop episodes of **jaundice**, which may only become evident in the context of a trigger (eg, illness, pregnancy, oral contraceptive use). Otherwise, they are usually asymptomatic with a normal physical examination.

Impaired bilirubin excretion may result in **direct (conjugated) hyperbilirubinemia** (eg, usually 2-5 mg/dL), but other routine laboratory tests (eg, complete blood count, liver function studies) are typically normal. Grossly, the liver appears black due to impaired excretion of epinephrine metabolites that accumulate within lysosomes.

**(Choice B)** Impaired bilirubin conjugation is seen in conditions such as Crigler-Najjar syndrome and Gilbert syndrome and results in indirect (unconjugated) hyperbilirubinemia.

**(Choice C)** Increased production of catecholamines is not associated with Dubin-Johnson syndrome despite the hepatocyte accumulation of epinephrine metabolites in this condition. Pheochromocytomas are catecholamine-secreting tumors of the adrenal medulla.

**(Choice D)** Ineffective intramedullary erythropoiesis is seen in conditions such as beta-thalassemia and myelodysplasia, and can result in indirect hyperbilirubinemia.





despite the hepatocyte accumulation of epinephrine metabolites in this condition. Pheochromocytomas are catecholamine-secreting tumors of the adrenal medulla.

**(Choice D)** Ineffective intramedullary erythropoiesis is seen in conditions such as beta-thalassemia and myelodysplasia, and can result in indirect hyperbilirubinemia.

**(Choice E)** Low levels of serum ceruloplasmin are seen in Wilson disease, which is typically associated with liver (eg, hepatitis, cirrhosis), psychiatric (eg, depression, personality changes), and neurologic (eg, dysarthria, movement disorder) abnormalities.

### Educational objective:

Dubin-Johnson syndrome is a benign disorder characterized by defective hepatic excretion of bilirubin glucuronides across the canalicular membrane, resulting in direct hyperbilirubinemia and jaundice.

Grossly, the liver appears black due to impaired excretion of epinephrine metabolites, which histologically appear as dense pigments within lysosomes.

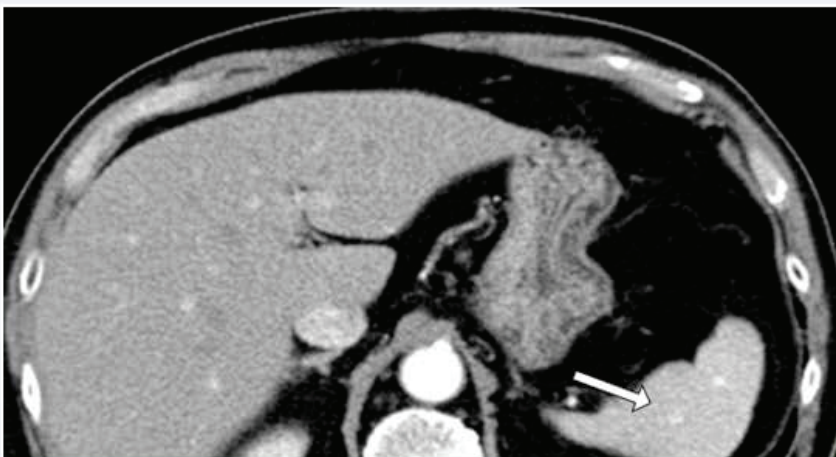
### References

- [Hyperbilirubinemia syndromes \(Gilbert-Meulengracht, Crigler-Najjar, Dubin-Johnson, and Rotor syndrome\).](#)





A 23-year-old man comes to the office with a 2-week history of malaise, loss of appetite, and vague abdominal pain. The patient has had no nausea, vomiting, changes in his bowel habits, dysuria, urinary frequency, or hematuria. He had an appendectomy for acute appendicitis at age 15; his medical history is otherwise unremarkable. He does not use tobacco or alcohol and has had no recent travel. His father was diagnosed with colon cancer at age 60. Physical examination reveals normal bowel sounds and no guarding or rebound tenderness. Abdominal CT scan obtained as part of this patient's evaluation is shown in the image below.







Item 7 of 40

Question Id: 12198



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

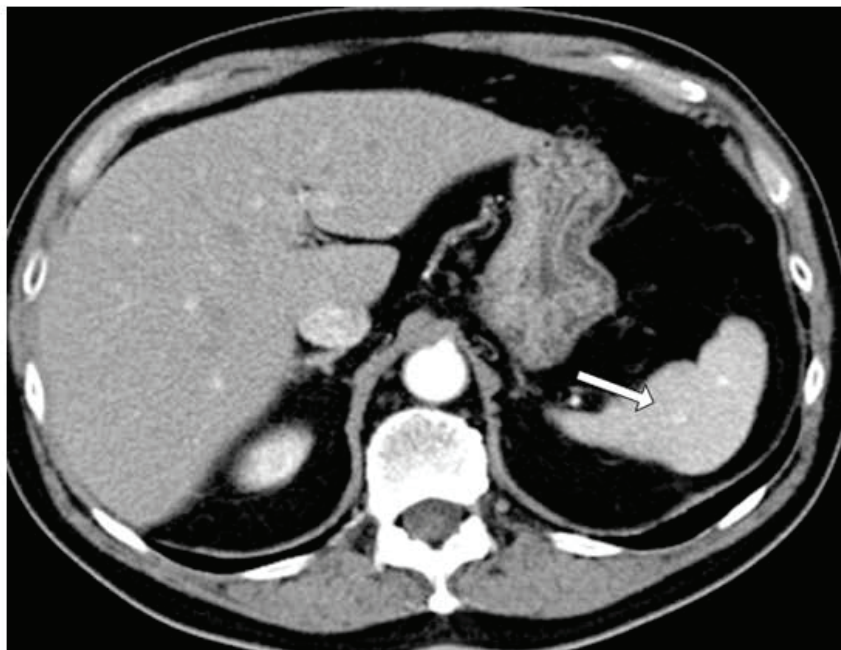


Text Zoom



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### Exhibit Display



Zoom In

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Block Time Remaining: 00:05:33

TUTOR

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Feedback



Suspend



End Block



The anatomical structure indicated by the arrow originates from which of the following embryologic divisions?

- ☐ A. Ectoderm
- ☐ B. Endoderm
- ☐ C. Mesoderm
- ☐ D. Neural crest
- ☐ E. Notochord

Submit





The anatomical structure indicated by the arrow originates from which of the following embryologic divisions?

- ☐ A. Ectoderm (2%)
- ☐ B. Endoderm (18%)
- ☒ C. Mesoderm (74%)
- ☐ D. Neural crest (4%)
- ☐ E. Notochord (0%)

Correct



74%

Answered correctly



13 secs

Time spent



01/31/2021

Last updated

Block Time Remaining: 00:05:42

TUTOR

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Feedback

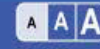


Suspend



End Block





## Embryological derivatives

Ectoderm	Surface ectoderm	<ul style="list-style-type: none"><li>• Anterior pituitary (Rathke pouch)</li><li>• Lens &amp; cornea</li><li>• Inner ear sensory organs, olfactory epithelium</li><li>• Nasal &amp; oral epithelial linings, salivary glands</li><li>• Epidermis, sweat &amp; mammary glands</li></ul>
	Neural tube	<ul style="list-style-type: none"><li>• Brain &amp; spinal cord</li><li>• Posterior pituitary, pineal gland</li><li>• Retina</li></ul>
	Neural crest	<ul style="list-style-type: none"><li>• Neural ganglia, adrenal medulla</li><li>• Schwann cells; pia &amp; arachnoid mater</li><li>• Aorticopulmonary septum &amp; endocardial cushions</li><li>• Branchial arches (bones &amp; cartilage)</li><li>• Skull bones</li><li>• Melanocytes</li></ul>
		<ul style="list-style-type: none"><li>• Muscles (skeletal, cardiac &amp; smooth)</li></ul>





Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

## Mesoderm

- Muscles (skeletal, cardiac & smooth)
- Connective tissue, bone & cartilage
- Serosal linings (eg, peritoneum)
- Cardiovascular & lymphatic system
- Spleen & hemopoietic cells
- Kidney & ureters, internal genitalia
- Adrenal cortex

## Endoderm

- Gastrointestinal tract, liver, pancreas
- Lungs
- Thymus, parathyroids, thyroid follicular cells
- Middle ear epithelium
- Bladder & urethra
- Parafollicular (C) cells\*

\*Formerly thought to be of neural crest origin.

The arrow in this patient's abdominal CT scan is pointing to the **spleen**, a large, wedge-shaped lymphatic organ that is situated in the **posterior superior** portion of the **left abdominal cavity**. While most gut





The arrow in this patient's abdominal CT scan is pointing to the **spleen**, a large, wedge-shaped lymphatic organ that is situated in the **posterior superior** portion of the **left abdominal cavity**. While most gut tissue is endodermal in origin, the spleen is unique as it is derived from condensed mesenchymal tissue in the dorsal mesentery during embryonic development. Mesenchymal tissue arises from the **mesoderm germ layer** and is characterized by loosely associated cells surrounded by the extracellular matrix.

**(Choice E)** The notochord is a mesodermally derived structure that almost completely regresses in humans, and its only major derivative is the nucleus pulposus of the intervertebral disc. Other major derivatives of the mesoderm germ layer include muscle, bone, lymphatics, the cardiovascular system, and kidneys/ureters.

### Educational objective:

The spleen is a large, wedge-shaped lymphatic organ that is situated in the posterior superior portion of the left abdominal cavity. It is derived from mesoderm in the dorsal mesentery during embryonic development.

### References

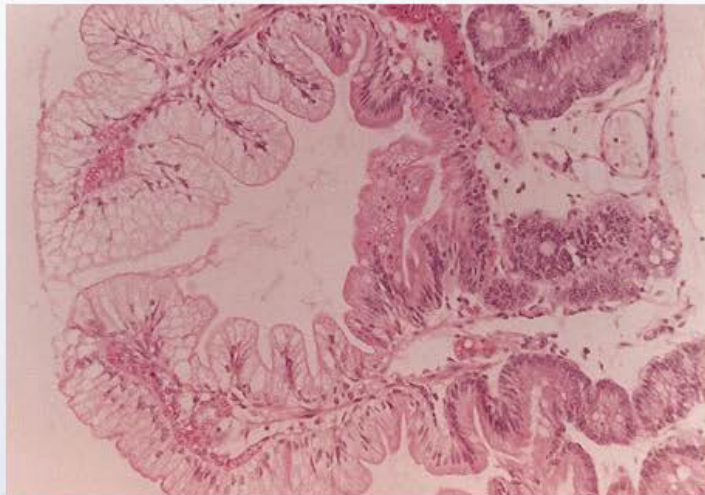
- [Embryonic origins of spleen asymmetry.](#)







A 5-month-old boy is being evaluated for poor weight gain since birth. He is noted to have bulky and greasy stools. A jejunal biopsy shows the findings seen in the slide below.



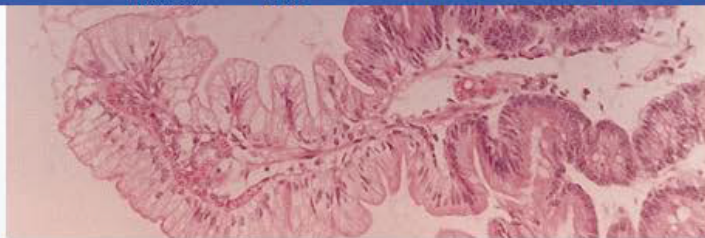
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This patient most likely suffers from which of the following conditions?

☐ A. Abetalipoproteinemia

☐ B. Celiac disease



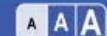


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This patient most likely suffers from which of the following conditions?

- ☐ A. Abetalipoproteinemia
- ☐ B. Celiac disease
- ☐ C. Chronic pancreatitis
- ☐ D. Crohn's disease
- ☐ E. Lactase deficiency
- ☐ F. Whipple disease
- ☐ G. Zollinger-Ellison syndrome





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This patient most likely suffers from which of the following conditions?

- ☒ A. Abetalipoproteinemia (40%)
- ☐ B. Celiac disease (24%)
- ☐ C. Chronic pancreatitis (3%)
- ☐ D. Crohn's disease (3%)
- ☐ E. Lactase deficiency (12%)
- ☐ F. Whipple disease (14%)
- ☐ G. Zollinger-Ellison syndrome (1%)

Correct

40%



12 secs



02/16/2021

Block Time Remaining: 00:05:54

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Feedback

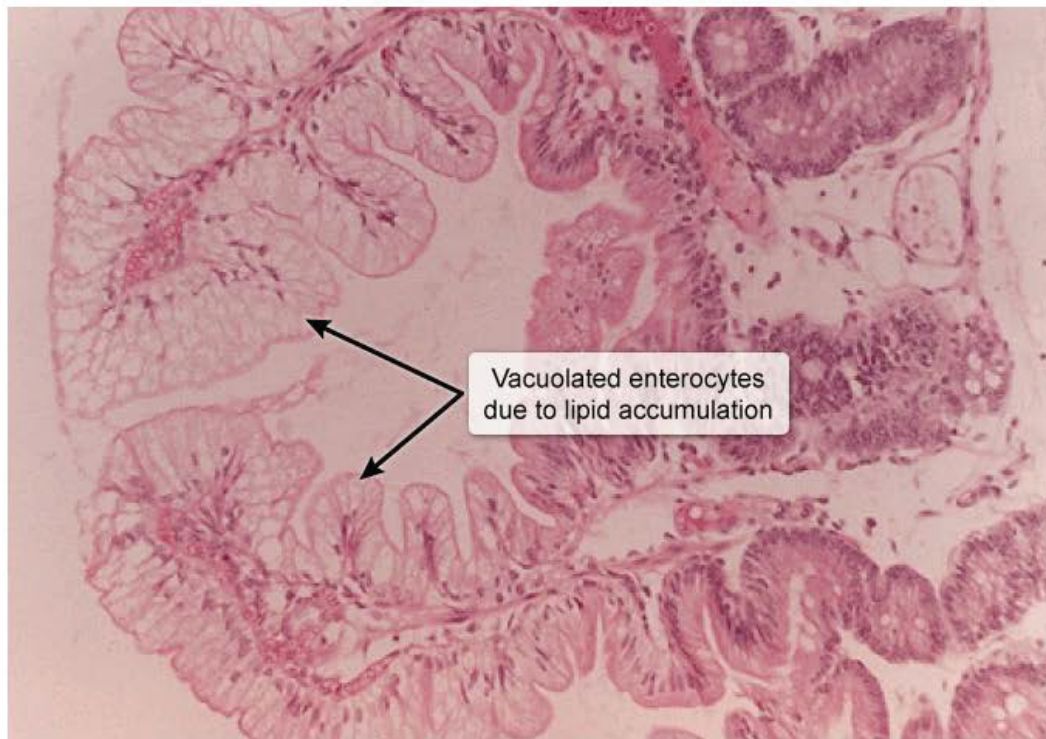
Suspend

End Block





## Abetalipoproteinemia





The slide above shows normal intestinal mucosal architecture, but the enterocytes contain clear or foamy cytoplasm (arrows) which is more prominent at the tips of the villi. These findings occur due to accumulation of lipids in the absorptive cells of the intestinal epithelium and are typical of abetalipoproteinemia, a disease caused by impaired formation of apolipoprotein B (apoB)-containing lipoproteins.

Dietary lipids are normally processed in small-bowel enterocytes and secreted as chylomicrons; endogenously produced lipids are secreted from liver hepatocytes as very low-density lipoprotein (VLDL). Chylomicron and VLDL particles are synthesized within the endoplasmic reticulum as lipids accumulate around a single apoB molecule. ApoB-100 is found in VLDL, and apoB-48 (a truncated version without the LDL receptor ligand) is present in chylomicrons. During the synthesis of apoB-containing lipoproteins, microsomal triglyceride transfer protein (MTP) functions as a chaperone protein necessary for proper folding of apoB and also participates in the transfer of lipids to newly formed chylomicrons and VLDL particles.

Abetalipoproteinemia is most commonly caused by an autosomal recessive, loss-of-function mutation in the **MTP gene**. It manifests during the first year of life with symptoms of malabsorption (eg, abdominal distention, foul-smelling stool). Laboratory studies show very low plasma triglyceride and cholesterol levels, and chylomicrons, VLDLs, and apoB are entirely absent from the blood. Poor lipid absorption







particles.

Abetalipoproteinemia is most commonly caused by an autosomal recessive, loss-of-function mutation in the **MTP gene**. It manifests during the first year of life with symptoms of malabsorption (eg, abdominal distention, foul-smelling stool). Laboratory studies show very low plasma triglyceride and cholesterol levels, and chylomicrons, VLDLs, and apoB are entirely absent from the blood. Poor lipid absorption causes deficiency of fat-soluble vitamins (particularly vitamin E) and essential fatty acids. This results in red blood cells with abnormal membranes and thorny projections called **acanthocytes** as well as multiple **neurologic abnormalities** (eg, progressive ataxia, retinitis pigmentosa).

**(Choice B)** Light microscopy shows atrophy and blunting of the villi in celiac disease. Chronic inflammatory infiltrate of the lamina propria is also present. None of these features are seen in the slide above.

**(Choices C, E, and G)** No abnormalities are found on light microscopy of the small intestine in chronic pancreatitis, Zollinger-Ellison syndrome, or lactase deficiency.

**(Choice D)** Light microscopy in [Crohn's disease](#) shows chronic inflammation of all layers of the intestinal wall and noncaseating granulomas.

**(Choice F)** The characteristic microscopic finding in [Whipple disease](#) is distended macrophages in the







**(Choices C, E, and G)** No abnormalities are found on light microscopy of the small intestine in chronic pancreatitis, Zollinger-Ellison syndrome, or lactase deficiency.

**(Choice D)** Light microscopy in **Crohn's disease** shows chronic inflammation of all layers of the intestinal wall and noncaseating granulomas.

**(Choice F)** The characteristic microscopic finding in **Whipple disease** is distended macrophages in the lamina propria of the small intestine. Macrophages contain PAS-positive and diastase-resistant granules and rod-shaped *Tropheryma whippelii* bacilli.

### Educational objective:

Abetalipoproteinemia is an inherited inability to synthesize apolipoprotein B, an important component of chylomicrons and very low-density lipoprotein. Lipids absorbed by the small intestine cannot be transported into the blood and accumulate in the intestinal epithelium, resulting in enterocytes with clear or foamy cytoplasm.

Pathology

Gastrointestinal &amp; Nutrition

Abetalipoproteinemia

Subject

System

Topic

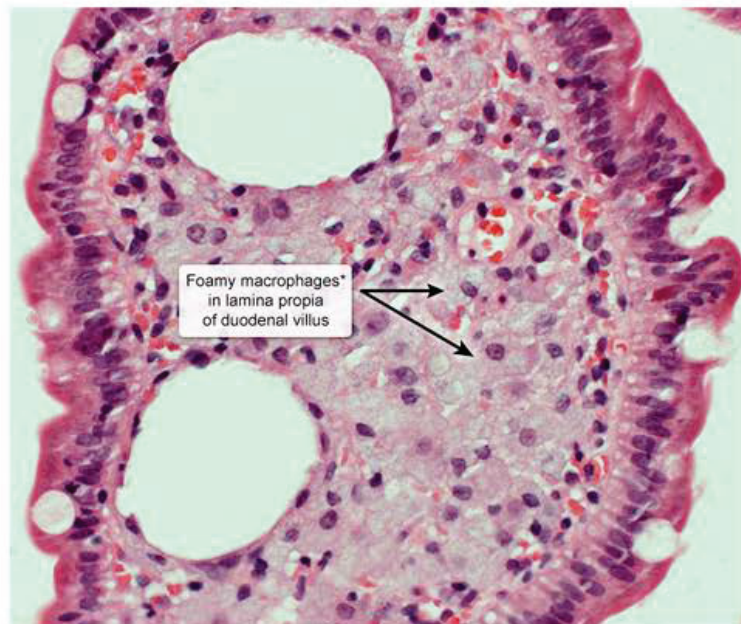
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(Choices C, E, and G) No abnormalities are found on light microscopy of the small intestine in chronic

## Exhibit Display

## Whipple disease



\*Contain Tropheryma whipplei

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Zoom In

Zoom Out

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A 23-year-old woman comes to the physician due to acute nausea and vomiting. She recently returned from a vacation to Mexico and started to feel "queasy" on the last day of her trip. The patient then developed nausea with frequent vomiting and intermittent bouts of watery diarrhea. She has no visible blood in her stools. Her temperature is 36.8 C (98 F), blood pressure is 118/70 mm Hg, pulse is 86/min, and respirations are 12/min. Abdominal examination shows mild tenderness and increased bowel sounds. Improvement of this patient's vomiting would best be achieved by a medication targeting which of the following receptors?

- ☐ A. 5-HT<sub>3</sub> receptor
- ☐ B.  $\mu$ -opioid receptor
- ☐ C. Dopamine receptor
- ☐ D. Histamine H<sub>1</sub> receptor
- ☐ E. Histamine H<sub>2</sub> receptor
- ☐ F. Muscarinic acetylcholine receptor
- ☐ G. Somatostatin receptor







developed nausea with frequent vomiting and intermittent bouts of watery diarrhea. She has no visible

blood in her stools. Her temperature is 36.8 C (98 F), blood pressure is 118/70 mm Hg, pulse is 86/min, and respirations are 12/min. Abdominal examination shows mild tenderness and increased bowel sounds. Improvement of this patient's vomiting would best be achieved by a medication targeting which of the following receptors?

- ☒ A. 5-HT<sub>3</sub> receptor (55%)
- ☐ B.  $\mu$ -opioid receptor (9%)
- ☒ C. Dopamine receptor (11%)
- ☐ D. Histamine H<sub>1</sub> receptor (5%)
- ☐ E. Histamine H<sub>2</sub> receptor (3%)
- ☐ F. Muscarinic acetylcholine receptor (13%)
- ☐ G. Somatostatin receptor (2%)

Incorrect

Correct answer



55%

Answered correctly



02 mins, 28 secs

Time spent



09/06/2020

Last updated

Block Time Remaining: 00:08:22

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Feedback



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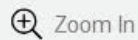
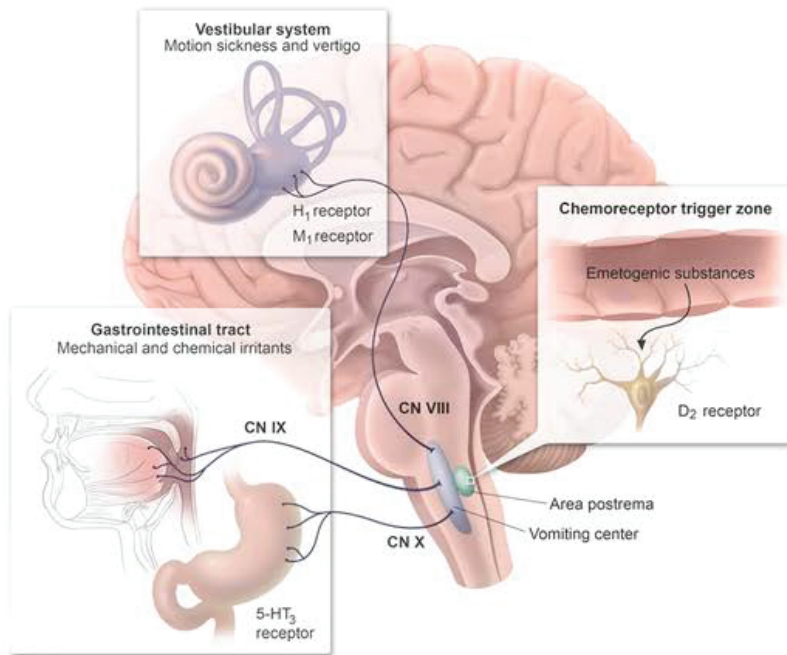


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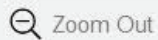


## Exhibit Display

## Physiologic causes of nausea



Zoom In



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This patient's nausea, vomiting, and watery diarrhea are typical symptoms of classic **travelers' diarrhea (TD)**. TD can be caused by a variety of organisms, including bacteria (eg, *Escherichia coli*), viruses (eg, rotaviruses), or occasionally, parasites (eg, *Cryptosporidium parvum*). In most cases, the illness is self-limited and treatment is symptomatic.

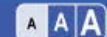
The choice of antiemetic therapy depends on the source of the emetogenic stimulus. Conditions that cause **gastrointestinal irritation** (eg, infections, chemotherapy, distention) result in increased mucosal **serotonin** release and activation of 5-HT<sub>3</sub> receptors on vagal and spinal afferent nerves. These then relay their impulses to the medullary vomiting center, inducing emesis. **5-HT<sub>3</sub> receptor antagonists** (eg, ondansetron) are well-tolerated medications that are very effective at reducing nausea and vomiting caused by gastrointestinal upset.

**(Choice B)** Loperamide is a  $\mu$ -opioid receptor agonist that functions as an antimotility agent. It is commonly used in TD to reduce diarrhea but can worsen nausea and vomiting due to colonic retention.

**(Choice C)** Dopamine receptor antagonists (eg, metoclopramide, prochlorperazine) are effective in treating central nausea (seen in acute migraines) and also reduce migraine headache pain. Dopamine antagonists have significant adverse effects including sedation and extrapyramidal symptoms: these are







**(Choice C)** Dopamine receptor antagonists (eg, metoclopramide, prochlorperazine) are effective in treating central nausea (seen in acute migraines) and also reduce migraine headache pain. Dopamine antagonists have significant adverse effects including sedation and extrapyramidal symptoms; these are not the first-line treatment for nausea due to gastrointestinal upset.

**(Choices D and F)** First-generation  $H_1$  receptor antagonists (eg, diphenhydramine, meclizine) and muscarinic acetylcholine receptor antagonists (eg, scopolamine) are frequently used to treat vestibular nausea (eg, motion sickness). Promethazine is a dopamine and  $H_1$  receptor antagonist that can also treat vestibular nausea. All of these medications can cause significant sedation.

**(Choice E)**  $H_2$  blockers (eg, ranitidine) reduce gastric acid secretion and can alleviate symptoms of gastroesophageal reflux but do not treat nausea and vomiting.

**(Choice G)** Somatostatin receptor agonists (eg, octreotide) inhibit bioactive amine release and are used to treat diarrhea in patients with carcinoid syndrome and vasoactive intestinal peptide-secreting tumors (ie, VIPoma). They are also used for treatment of acute esophageal variceal hemorrhage.

### Educational objective:

5-HT<sub>3</sub> receptor antagonists are useful for the treatment of visceral nausea due to gastrointestinal insults, such as gastroenteritis, chemotherapy, and general anesthesia. Antihistamines and anticholinergics are





**(Choices D and F)** First-generation  $H_1$  receptor antagonists (eg, diphenhydramine, meclizine) and muscarinic acetylcholine receptor antagonists (eg, scopolamine) are frequently used to treat vestibular nausea (eg, motion sickness). Promethazine is a dopamine and  $H_1$  receptor antagonist that can also treat vestibular nausea. All of these medications can cause significant sedation.

**(Choice E)**  $H_2$  blockers (eg, ranitidine) reduce gastric acid secretion and can alleviate symptoms of gastroesophageal reflux but do not treat nausea and vomiting.

**(Choice G)** Somatostatin receptor agonists (eg, octreotide) inhibit bioactive amine release and are used to treat diarrhea in patients with carcinoid syndrome and vasoactive intestinal peptide-secreting tumors (ie, VIPoma). They are also used for treatment of acute esophageal variceal hemorrhage.

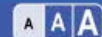
### Educational objective:

5-HT<sub>3</sub> receptor antagonists are useful for the treatment of visceral nausea due to gastrointestinal insults, such as gastroenteritis, chemotherapy, and general anesthesia. Antihistamines and anticholinergics are recommended for vestibular nausea. Dopamine antagonists are useful for nausea associated with migraine.

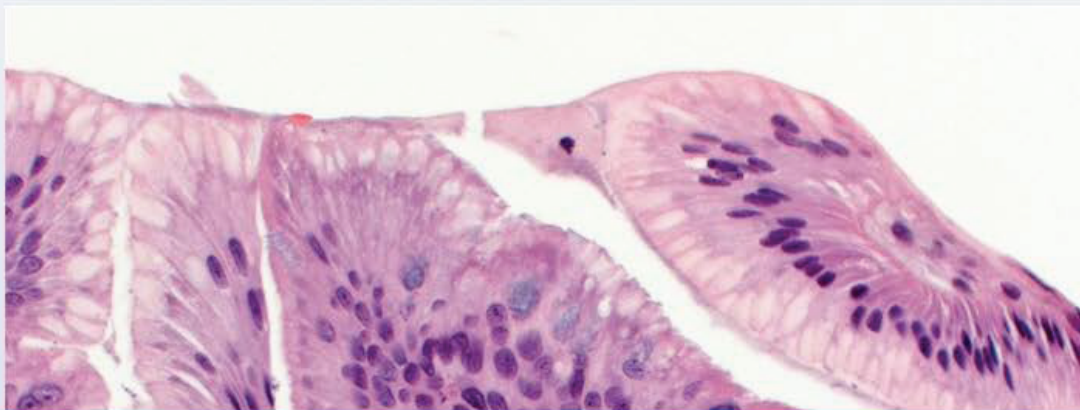
### References



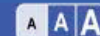




A 49-year-old man comes to the office for evaluation of a dry cough that occurs mainly at night. His symptoms have been present on and off for several years, but he has not been previously evaluated. The patient also reports a frequent sore throat and occasional epigastric discomfort. He has tried a variety of antihistamines and over-the-counter cough medications without relief. Past medical history is notable for obesity and diet-controlled type 2 diabetes mellitus. He does not smoke or drink alcohol. Cardiopulmonary and abdominal examinations are unremarkable. Chest x-ray reveals no abnormalities, and pulmonary function testing is normal. The patient undergoes upper gastrointestinal endoscopy with mucosal biopsies. Microscopic findings on lower esophageal biopsy are shown in the image below.

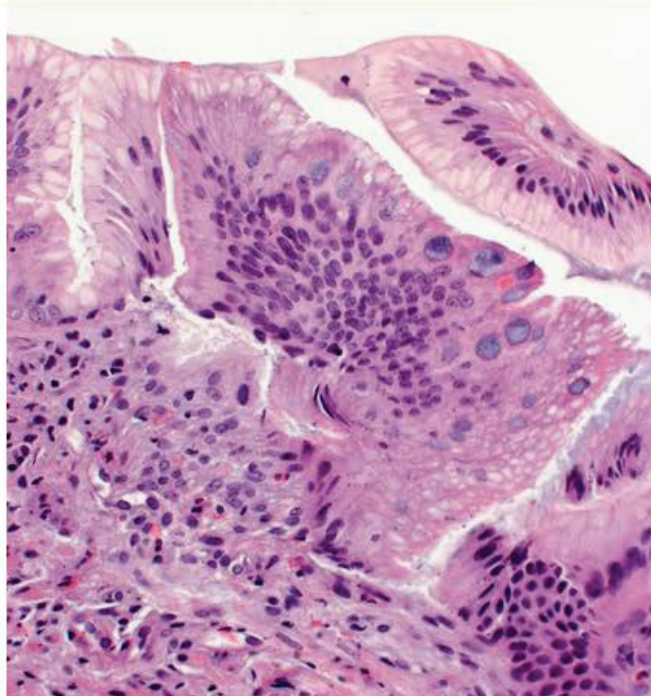






microscopic findings on lower esophageal biopsy are shown in the image below.

## Exhibit Display



Zoom In

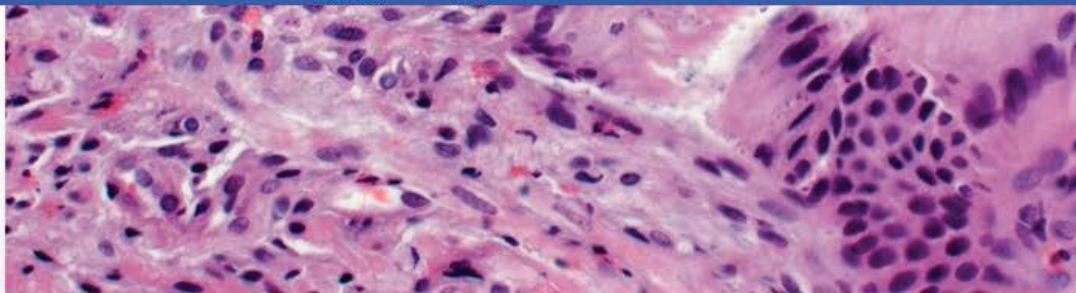
Zoom Out

Reset

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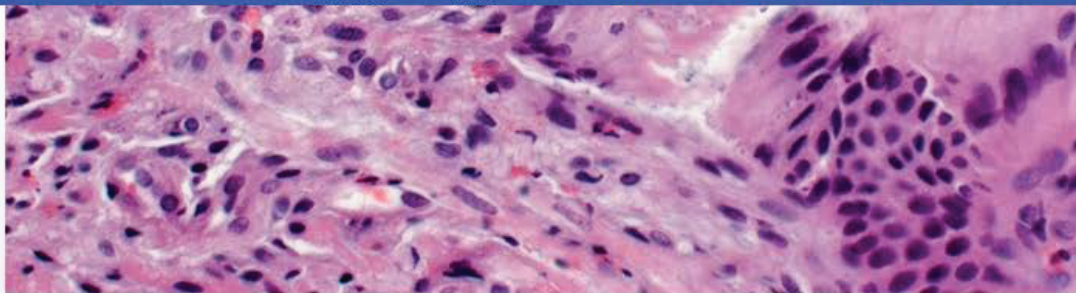


This patient is at highest risk of which of the following complications?

- ☐ A. Achalasia
- ☐ B. Adenocarcinoma
- ☐ C. Crohn disease
- ☐ D. Squamous cell carcinoma
- ☐ E. Variceal bleeding

Submit





This patient is at highest risk of which of the following complications?

- ☐ A. Achalasia (1%)
- ☒ B. Adenocarcinoma (88%)
- ☐ C. Crohn disease (0%)
- ☐ D. Squamous cell carcinoma (7%)
- ☐ E. Variceal bleeding (0%)

Correct

88%



52 secs



01/05/2021

Block Time Remaining: 00:09:14

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Feedback



Suspend



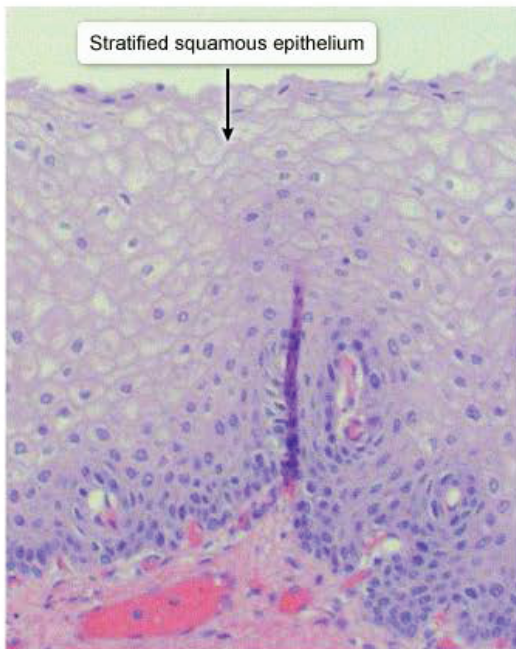
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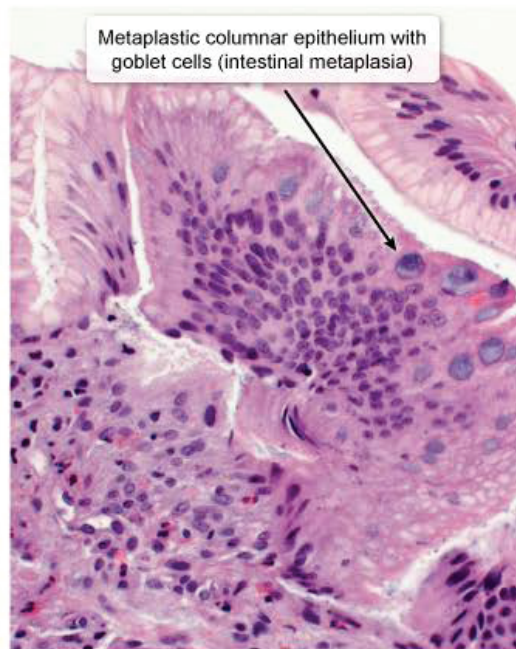


## Exhibit Display

## Normal esophagus



## Barrett esophagus



Zoom In



Zoom Out



Reset



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This patient's persistent dry cough, sore throat, and epigastric discomfort is suggestive of **gastroesophageal reflux disease**. His esophageal biopsy shows intestinal-type columnar epithelium with goblet cells where a normal esophagus would be lined by stratified squamous epithelium. This finding is diagnostic of **Barrett esophagus**, which is seen when acidic gastric contents enter the esophagus, causing inflammation and subsequent epithelial necrosis.

Sustained epithelial damage promotes metaplastic replacement of the normal stratified squamous epithelium with **intestinal-type columnar cells**. The transition to columnar epithelium may be seen grossly on endoscopy as tongues of beefy red mucosa extending above the lower esophageal sphincter into areas of normal pale pink squamous mucosa.

People with severe and **long-standing acid reflux** are most prone to Barrett esophagus. This metaplasia is hypothesized to be adaptive at first, as intestinal-type epithelium is more resistant to gastric acid. However, it is a major risk factor for **esophageal adenocarcinoma**, which typically develops from the metaplastic intestinal epithelium in the distal part of the esophagus.

**(Choices A and D)** The major risk factors for squamous cell carcinoma of the esophagus are cigarette smoking and alcohol use. Achalasia, an esophageal motility disorder caused by the loss of ganglion cells







is hypothesized to be adaptive at first, as intestinal-type epithelium is more resistant to gastric acid.

However, it is a major risk factor for **esophageal adenocarcinoma**, which typically develops from the metaplastic intestinal epithelium in the distal part of the esophagus.

**(Choices A and D)** The major risk factors for squamous cell carcinoma of the esophagus are cigarette smoking and alcohol use. Achalasia, an esophageal motility disorder caused by the loss of ganglion cells in the lower esophagus, also carries an increased risk of squamous carcinoma.

**(Choices C and E)** Crohn disease can affect the esophagus, typically causing patchy inflammation, erosions, ulcers, strictures, and fistulas. Esophageal varices develop in the context of high portal venous pressure, most often due to alcoholic or post-viral liver cirrhosis. These conditions are not associated with Barrett esophagus.

### Educational objective:

Barrett esophagus is a metaplastic condition in which the normal squamous epithelium of the distal esophagus is replaced by intestinal-type columnar epithelium. It occurs most often in longstanding acid reflux and is associated with an increased risk of adenocarcinoma.

Pathology

Gastrointestinal & Nutrition

Barretts esophagus







A 52-year-old man is brought to the emergency department due to repeated vomiting that began 2 hours ago. His vomit is dark brown and has a granular consistency. The patient has a history of dyspepsia, for which he takes over-the-counter antacids as needed and degenerative knee arthritis, for which he takes naproxen regularly. He drinks 2-3 beers daily. Temperature is 36.7 C (98 F), blood pressure is 114/62 mm Hg, pulse is 102/min, and respirations are 14/min. Physical examination reveals mild epigastric tenderness with no rebound or guarding. Hemoglobin is 9 g/dL. Endoscopy shows a deep, bleeding ulcer on the posterior wall of the duodenal bulb. This patient's ulcer has most likely penetrated which of the following arteries?

- ☐ A. Common hepatic
- ☐ B. Gastroduodenal
- ☐ C. Inferior pancreaticoduodenal
- ☒ D. Left gastroepiploic
- ☐ E. Right gastric
- ☐ F. Splenic





ago. His vomit is dark brown and has a granular consistency. The patient has a history of dyspepsia, for which he takes over-the-counter antacids as needed and degenerative knee arthritis, for which he takes naproxen regularly. He drinks 2-3 beers daily. Temperature is 36.7 C (98 F), blood pressure is 114/62 mm Hg, pulse is 102/min, and respirations are 14/min. Physical examination reveals mild epigastric tenderness with no rebound or guarding. Hemoglobin is 9 g/dL. Endoscopy shows a deep, bleeding ulcer on the posterior wall of the duodenal bulb. This patient's ulcer has most likely penetrated which of the following arteries?

- ☐ A. Common hepatic
- ☐ B. Gastroduodenal
- ☐ C. Inferior pancreaticoduodenal
- ☐ D. Left gastroepiploic
- ☐ E. Right gastric
- ☐ F. Splenic
- ☐ G. Superior mesenteric





naproxen regularly. He drinks 2-3 beers daily. Temperature is 36.7 C (98 F), blood pressure is 114/62 mm Hg, pulse is 102/min, and respirations are 14/min. Physical examination reveals mild epigastric tenderness with no rebound or guarding. Hemoglobin is 9 g/dL. Endoscopy shows a deep, bleeding ulcer on the posterior wall of the duodenal bulb. This patient's ulcer has most likely penetrated which of the following arteries?

- ☐ A. Common hepatic (1%)
- ☒ B. Gastroduodenal (78%)
- ☐ C. Inferior pancreaticoduodenal (10%)
- ☐ D. Left gastroepiploic (2%)
- ☐ E. Right gastric (3%)
- ☐ F. Splenic (1%)
- ☐ G. Superior mesenteric (1%)

Correct

78%

21 secs

09/01/2020

Block Time Remaining: 00:09:35

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Feedback



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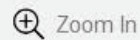
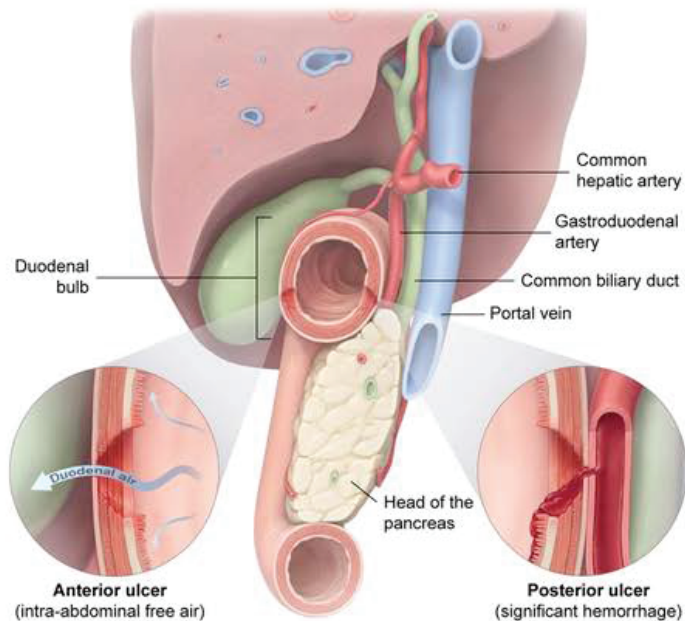
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## Exhibit Display

## Duodenal ulcers and surrounding anatomy



Zoom In



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My Notebook





(intra-abdominal free air)

(significant hemorrhage)

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Bleeding peptic ulcer disease should be considered in patients who develop acute epigastric pain, unstable vital signs, or hematemesis, particularly in the setting of prior dyspepsia. Most peptic ulcers are caused by *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug use; other risk factors include smoking, older age, and glucocorticoid use.

Duodenal ulcers are more common than gastric ulcers and tend to occur anteriorly. Ulcers located on the anterior wall of the duodenal bulb are more prone to perforation; those on the posterior wall are more likely to cause hemorrhage. These complications are explained by the relationship of the duodenal bulb to adjacent organs. The duodenal bulb is approximately 5 cm long, beginning at the pylorus and ending at the neck of the gallbladder. The gallbladder and liver lie anterior to the duodenal bulb within the intraperitoneal space; the gastroduodenal artery, common biliary duct, and portal vein are posterior to the bulb; and the head of the pancreas is located inferiorly.

When an ulcer penetrates the **posterior duodenal wall**, it is likely to erode into the **gastroduodenal artery**, which perfuses both the pylorus and the proximal part of the duodenum. Damage to the gastroduodenal artery can cause significant **upper gastrointestinal bleeding**.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



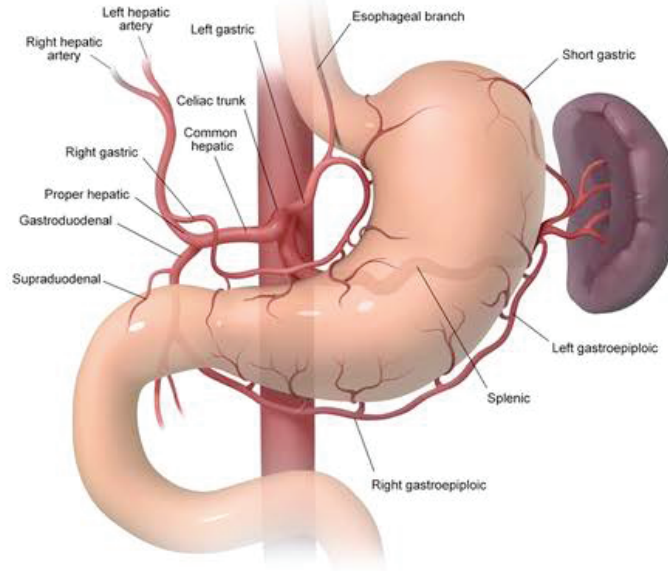
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(intra-abdominal free air)

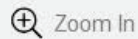
(significant hemorrhage)

## Exhibit Display

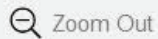
## Upper abdominal vasculature



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Zoom In



Zoom Out



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Feedback



Suspend



End Block





**(Choice A)** The common hepatic artery arises from the celiac trunk and bifurcates into the proper hepatic and gastroduodenal arteries. It passes superior to the duodenal bulb.

**(Choice C)** The inferior pancreaticoduodenal artery is a branch of the superior mesenteric artery. It supplies blood to the lower duodenum and to the head of the pancreas. This artery has no close relation to the duodenal bulb.

**(Choices D, E, and F)** The left gastroepiploic and right gastric arteries supply blood to the greater and lesser curves of the stomach, respectively. The short gastric arteries arise off the splenic artery and supply the upper portions of the greater curvature. These vessels do not lie in close proximity to the duodenal bulb.

**(Choice G)** The superior mesenteric artery lies anterior to the transverse part of the duodenum. It arises from the anterior surface of the abdominal aorta and supplies the intestine from the duodenum to the proximal two-thirds of the transverse colon.

### Educational objective:

The gastroduodenal artery lies along the posterior wall of the duodenal bulb and is likely to be eroded by posterior duodenal ulcers. Ulceration into the gastroduodenal artery can be a source of life-threatening hemorrhage.





A 42-year-old man comes to the office due to leg swelling. He has also had yellowing of the eyes and progressive abdominal distension for the past 3 weeks, as well as an associated 7-kg (15.4-lb) weight gain. The patient drinks at least 8 beers a day and in the past has been admitted to the hospital for intoxication and seizures. He denies smoking or intravenous drug use. Vital signs are within normal limits. Scleral icterus, spider angiomas, and palmar erythema are present. There is no jugular venous distension, and cardiac auscultation reveals a normal rate and rhythm. Breath sounds are normal. The abdomen is diffusely enlarged, and a fluid wave is easily elicited. Pitting edema is present in the bilateral lower extremities. Which of the following pathophysiologic changes is most likely present in this patient?

- |                          | Plasma oncotic pressure | Splanchnic vascular resistance | Effective arterial blood volume | Capillary permeability |
|--------------------------|-------------------------|--------------------------------|---------------------------------|------------------------|
| <input type="radio"/> A. | ↓                       | ↓                              | ↓                               | Normal                 |
| <input type="radio"/> B. | Normal                  | ↑                              | ↓                               | Normal                 |
| <input type="radio"/> C. | ↓                       | Normal                         | ↑                               | ↑                      |





intoxication and seizures. He denies smoking or intravenous drug use. Vital signs are within normal limits.

Scleral icterus, spider angiomas, and palmar erythema are present. There is no jugular venous distension, and cardiac auscultation reveals a normal rate and rhythm. Breath sounds are normal. The abdomen is diffusely enlarged, and a fluid wave is easily elicited. Pitting edema is present in the bilateral lower extremities. Which of the following pathophysiologic changes is most likely present in this patient?

	Plasma oncotic pressure	Splanchnic vascular resistance	Effective arterial blood volume	Capillary permeability
<input type="radio"/> A.	↓	↓	↓	Normal
<input type="radio"/> B.	Normal	↑	↓	Normal
<input type="radio"/> C.	↓	Normal	↑	↑
<input type="radio"/> D.	Normal	Normal	Normal	↑
<input type="radio"/> E.	↑	↓	Normal	Normal

**Submit**

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Feedback



Suspend



End Block



Sclerotic, spider angiomas, and palmar erythema are present. There is no jugular venous distension, and cardiac auscultation reveals a normal rate and rhythm. Breath sounds are normal. The abdomen is diffusely enlarged, and a fluid wave is easily elicited. Pitting edema is present in the bilateral lower extremities. Which of the following pathophysiologic changes is most likely present in this patient?

	Plasma oncotic pressure	Splanchnic vascular resistance	Effective arterial blood volume	Capillary permeability	
✓ <input checked="" type="radio"/> A.	↓	↓	↓	Normal	(63%)
<input type="radio"/> B.	Normal	↑	↓	Normal	(6%)
<input type="radio"/> C.	↓	Normal	↑	↑	(24%)
<input type="radio"/> D.	Normal	Normal	Normal	↑	(1%)
<input type="radio"/> E.	↑	↓	Normal	Normal	(3%)

Correct

63%  
Answered correctly

41 secs  
Time Spent

09/23/2020  
Last Updated

Block Time Remaining: 00:10:16  
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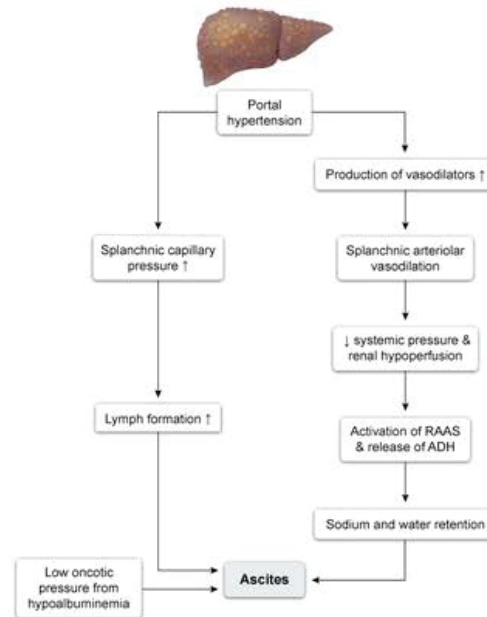
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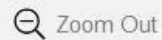
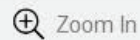
### Exhibit Display

#### Pathogenesis of ascites in cirrhosis



ADH = antidiuretic hormone; RAAS = renin-angiotensin-aldosterone system.

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ADH = antidiuretic hormone; RAAS = renin-angiotensin-aldosterone system.

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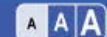
This patient has **ascites**, characterized by the accumulation of fluid within the peritoneal cavity. Ascites may occur in a variety of diseases (eg, peritoneal metastasis, congestive heart failure); however, in this patient with a history of heavy alcohol use and stigmata of chronic liver disease (eg, jaundice, spider angiomas, palmar erythema), it likely occurred from **cirrhosis**.

Cirrhosis is characterized by progressive liver fibrosis, which results in the formation of a high-resistance system (ie, **portal hypertension**). This results in the following alterations:

1. Nitric oxide is released, possibly due to stimulation by bacterial products (eg, endotoxin), which can more easily translocate from the gastrointestinal tract due to reduced host defenses (eg, impaired reticuloendothelial function) and portosystemic shunt formation (eg, decreased toxin clearance).
2. Splanchnic vasodilation occurs as a result, which **decreases the splanchnic vascular resistance** and **lowers the effective arterial blood volume** (EABV) due to blood pooling in the splanchnic vascular bed.
3. Low perfusion pressure results in activation of the **renin-angiotensin-aldosterone system** along with increased secretion of antidiuretic hormone, leading to **retention of sodium and water**.







Additionally, cirrhosis results in impaired synthetic function, leading to hypoalbuminemia and **low plasma oncotic pressure**, which reduces fluid resorption from the interstitium. Paired with portal hypertension (ie, increased hydrostatic pressure), these changes result in a vicious cycle of hypervolemia and third spacing, promoting the formation of ascites and peripheral edema. The capillaries remain physiologically normal, so **permeability is unchanged**.

**(Choice B)** Congestive heart failure causes low EABV (due to low cardiac output) with a consequent increase in sympathetic tone that results in increased splanchnic vascular resistance. Oncotic pressure and capillary permeability are unaffected.

**(Choice C)** Nephrotic syndrome causes edema due to increased permeability of the glomerular capillary wall, leading to loss of albumin, which decreases capillary oncotic pressure. Most patients also have a defect in sodium excretion from the kidneys, resulting in sodium retention and increased EABV. Splanchnic vascular resistance is unaffected.

**(Choice D)** Localized allergic reactions (eg, insect sting) can lead to increased capillary permeability, leading to dermal edema. Oncotic pressures, splanchnic vascular resistance, and EABV are unaffected.

**(Choice E)** Increased capillary oncotic pressure tends to inhibit fluid accumulation in the interstitial spaces, thereby decreasing peripheral edema and ascites.



and capillary permeability are unaffected.

**(Choice C)** Nephrotic syndrome causes edema due to increased permeability of the glomerular capillary wall, leading to loss of albumin, which decreases capillary oncotic pressure. Most patients also have a defect in sodium excretion from the kidneys, resulting in sodium retention and increased EABV. Splanchnic vascular resistance is unaffected.

**(Choice D)** Localized allergic reactions (eg, insect sting) can lead to increased capillary permeability, leading to dermal edema. Oncotic pressures, splanchnic vascular resistance, and EABV are unaffected.

**(Choice E)** Increased capillary oncotic pressure tends to inhibit fluid accumulation in the interstitial spaces, thereby decreasing peripheral edema and ascites.

### Educational objective:

Ascites in cirrhosis develops from hemodynamic changes related to portal hypertension. Splanchnic vasodilation decreases the splanchnic vascular resistance and lowers the effective arterial blood volume, which causes activation of the renin-angiotensin-aldosterone system and promotes sodium and water retention. Additionally, low oncotic pressure (ie, hypoalbuminemia due to impaired hepatic function) reduces fluid resorption from the interstitium.

### References



A 64-year-old man comes to the emergency department after an episode of hematemesis. He also reports dark stools and abdominal pain for the past several days. The patient has a history of chronic pancreatitis. Abdominal examination shows epigastric tenderness to palpation. Rectal examination is notable for black, guaiac-positive feces. Upper gastrointestinal endoscopy reveals a bleeding spot within a cluster of enlarged tortuous veins in the gastric fundus. The rest of the stomach and esophagus appears normal. Increased pressure in which of the following vascular structures is the most likely cause of this patient's condition?

- ☐ A. Azygos vein
- ☐ B. Left gastric vein
- ☐ C. Pancreaticoduodenal vein
- ☐ D. Splenic vein
- ☐ E. Superior mesenteric vein

**Submit**





Item 13 of 40

Question Id: 11795



Mark

Previous

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Tutorial

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Notes

Calculator

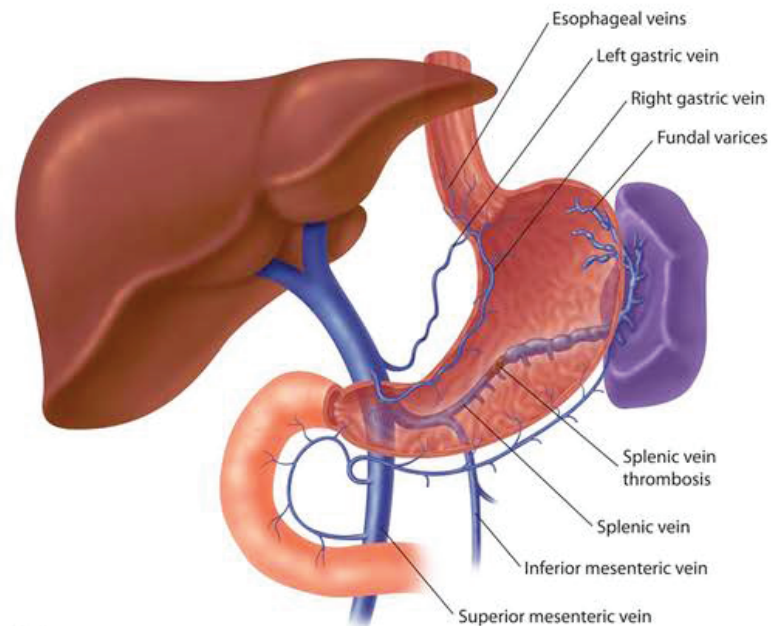
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Settings

### Exhibit Display

#### Splenic vein thrombosis



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Zoom In

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Reset

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Block Time Remaining: 00:10:32

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Feedback

Suspend

End Block



Gastric varices are dilated submucosal veins that can cause life-threatening bleeding in the upper gastrointestinal tract. The varices are commonly due to portal hypertension, which can be a complication of cirrhosis. Gastric varices can also be seen with **splenic vein thrombosis** due to chronic pancreatitis, pancreatic cancer, and abdominal tumors. The splenic vein runs along the posterior surface of the pancreas and can develop a blood clot from pancreatic inflammation. The **short gastric veins** drain the fundus of the stomach into the splenic vein. Splenic vein thrombosis can increase pressure in the short gastric veins and cause **gastric varices** only in the **fundus**. The rest of the stomach and esophagus are usually not affected.

**(Choice A)** The azygos vein drains blood from the esophageal veins into the superior vena cava. The formation of esophageal varices in the setting of portal hypertension provides collateral drainage from the portal venous system to the azygos system. The azygos vein also provides collateral circulation between the superior and inferior vena cava and can become enlarged with caval obstruction.

**(Choice B)** The left gastric vein drains blood from the upper stomach and lower esophagus into the portal vein. Portal hypertension can increase pressure in the left gastric veins and usually causes both gastric and esophageal varices.

**(Choices C and E)** The pancreaticoduodenal vein drains the pancreas and duodenum into the superior





the superior and inferior vena cava and can become enlarged with caval obstruction.

**(Choice B)** The left gastric vein drains blood from the upper stomach and lower esophagus into the portal vein. Portal hypertension can increase pressure in the left gastric veins and usually causes both gastric and esophageal varices.

**(Choices C and E)** The pancreaticoduodenal vein drains the pancreas and duodenum into the superior mesenteric vein (SMV). The SMV also drains blood from the lower stomach (via the right gastroepiploic vein) and small intestine. Blockage of the SMV could lead to variceal formation in the lower stomach, but not the upper regions.

### Educational objective:

The short gastric veins drain blood from the gastric fundus into the splenic vein. Pancreatic inflammation (eg, pancreatitis, pancreatic cancer) can cause a blood clot within the splenic vein, which can increase pressure in the short gastric veins and lead to gastric varices only in the fundus.

### References

- [Repeated pancreatitis-induced splenic vein thrombosis leads to intractable gastric variceal bleeding: A case report and review.](#)







A 5-month-old boy is brought to the emergency department due to poor feeding, weakness, and complete loss of extremity muscle tone. Vaccinations are up to date, and there is no significant medical history. The patient receives formula as his sole source of nutrition except for occasional fruit juice and honey. Which of the following is most likely to confirm the diagnosis in this patient?

- ☐ A. Blood test for liver enzymes
- ☐ B. Blood test for viral titers
- ☐ C. Stool test for bacterial toxins
- ☐ D. Stool test for occult blood
- ☐ E. Urine test for amino acids
- ☐ F. Urine test for glucose and ketones

Submit





A 5-month-old boy is brought to the emergency department due to poor feeding, weakness, and complete loss of extremity muscle tone. Vaccinations are up to date, and there is no significant medical history. The patient receives formula as his sole source of nutrition except for occasional fruit juice and honey. Which of the following is most likely to confirm the diagnosis in this patient?

- ☐ A. Blood test for liver enzymes (5%)
- ☐ B. Blood test for viral titers (0%)
- ☒ C. Stool test for bacterial toxins (80%)
- ☐ D. Stool test for occult blood (0%)
- ☐ E. Urine test for amino acids (4%)
- ☐ F. Urine test for glucose and ketones (7%)

Correct



80%  
Answered correctly

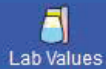


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Time Spent



12/06/2020  
Last Updated





## Infant botulism

### Pathogenesis

- Ingestion of *Clostridium botulinum* spores (eg, environmental dust/soil, honey)
- Spores colonize gastrointestinal tract & produce botulinum toxin
- Botulinum toxin inhibits presynaptic acetylcholine release

### Clinical presentation

- Age <12 months
- Constipation, poor feeding, hypotonia
- Oculobulbar palsies (eg, absent gag reflex, ptosis)
- Symmetric, descending flaccid paralysis

### Diagnosis

- Classic presentation
- Confirmation by identification of stool *C botulinum* spores or toxins

This 5-month-old patient has consumed **honey**, a food notorious for contamination with ***Clostridium botulinum*** spores. When an infant consumes *C botulinum* spores, the bacteria can germinate in the gastrointestinal tract. Bacteriolysis releases **botulinum toxin**, which is absorbed systemically and blocks release of **acetylcholine** from cholinergic presynaptic terminals.

Constipation is usually the first manifestation of **infant botulism**, followed days to weeks later by **mild weakness, lethargy, and reduced feeding**. In rare, severe cases, infants can have weakened suckling.







release of **acetylcholine** from cholinergic presynaptic terminals.

Constipation is usually the first manifestation of **infant botulism**, followed days to weeks later by **mild weakness**, lethargy, and **reduced feeding**. In rare, severe cases, infants can have weakened suckling and crying, diminished gag reflex, and symmetric, descending flaccid paralysis with loss of head control that can cause the infant to appear "floppy." In contrast, adult botulism usually results from ingestion of preformed toxin (eg, contaminated canned foods) and is almost always very severe.

While infant botulism can be diagnosed based on the clinical presentation and food consumption history, the diagnosis is usually confirmed through identification of *C botulinum* spores or **toxin in stool** samples.

**(Choice A)** Measurement of blood liver enzyme levels can indicate damage to hepatic cells in hereditary fructose intolerance (genetic deficiency in aldolase B). Although patients with fructose intolerance can have poor feeding shortly after juice and honey are added to the diet, other classic manifestations include hypoglycemia, vomiting, and hepatomegaly rather than loss of extremity muscle tone.

**(Choice B)** Serum viral titers are frequently used in the evaluation of patients with viral hepatitis or suspected Epstein-Barr or cytomegalovirus infections. Poor feeding with loss of extremity muscle tone is more characteristic of infant botulism.

**(Choice D)** Allergic proctocolitis in infants can present after introduction of different food groups, and the



suspected Epstein-Barr or cytomegalovirus infections. Poor feeding with loss of extremity muscle tone is more characteristic of infant botulism.

**(Choice D)** Allergic proctocolitis in infants can present after introduction of different food groups, and the diagnosis can be supported by stool studies that are positive for gross or occult blood. However, these infants usually appear well despite persistent diarrhea and/or rectal bleeding.

**(Choice E)** Patients with amino acids in their urine may have an inborn error of metabolism (eg, maple syrup urine disease) with symptoms usually manifesting in the neonatal period or early infancy.

**(Choice F)** High levels of urine glucose and ketones, together with hyperglycemia and metabolic acidosis, can support a diagnosis of diabetic ketoacidosis.

**Educational objective:**

Infant botulism can result from consumption of honey, which frequently contains *C botulinum* spores that can germinate and produce botulinum toxin. Symptoms of infant botulism include constipation, mild weakness, lethargy, poor feeding, and, in severe cases, flaccid paralysis. The diagnosis can be confirmed by identification of *C botulinum* spores or toxins in the stool.

Microbiology      Gastrointestinal & Nutrition      Botulism  
Subject      System      Topic

Block Time Remaining: 00:11:01

<https://t.me/USMLEWorldStep1>





A 68-year-old woman comes to the emergency department due to a 2-day history of crampy abdominal pain and vomiting. The patient has had no hematemesis, melena, or hematochezia. She has a history of hypertension, type 2 diabetes mellitus, and coronary artery disease. Several months ago, the patient had an episode of acute calculous cholecystitis that was managed non-operatively. Physical examination shows a distended, tympanic abdomen with high-pitched bowel sounds. Abdominal x-ray reveals air in the gallbladder and biliary tree. This patient's gallstone has most likely lodged in which of the following sites?

- ☐ A. Common bile duct
- ☐ B. Cystic duct
- ☐ C. Duodenum
- ☐ D. Ileum
- ☐ E. Jejunum

Submit







A 68-year-old woman comes to the emergency department due to a 2-day history of crampy abdominal pain and vomiting. The patient has had no hematemesis, melena, or hematochezia. She has a history of hypertension, type 2 diabetes mellitus, and coronary artery disease. Several months ago, the patient had an episode of acute calculous cholecystitis that was managed non-operatively. Physical examination shows a distended, tympanic abdomen with high-pitched bowel sounds. Abdominal x-ray reveals air in the gallbladder and biliary tree. This patient's gallstone has most likely lodged in which of the following sites?

- ☐ A. Common bile duct (24%)
- ☐ B. Cystic duct (11%)
- ☐ C. Duodenum (17%)
- ☒ D. Ileum (44%)
- ☐ E. Jejunum (1%)

Correct

44%  
Answered correctly

36 secs  
Time Spent

10/31/2020  
Last Updated

Block Time Remaining: 00:11:37

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



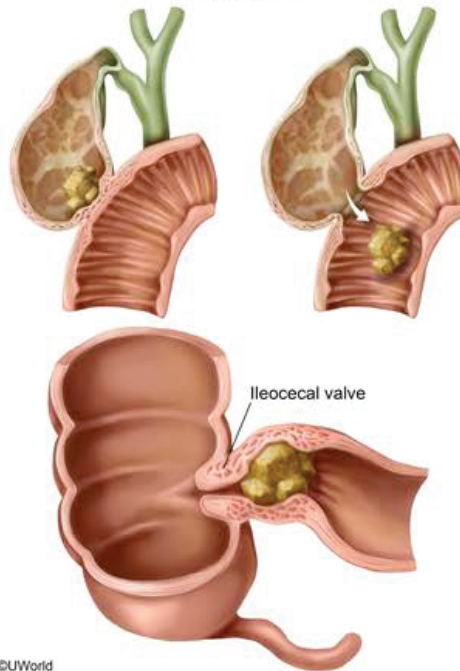
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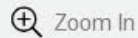
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## Exhibit Display

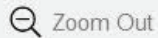
Gallstone ileus



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Zoom In



Zoom Out



Reset



New



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My Notebook

My Notebook

Block Time Remaining: 00:11:37

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Feedback



Suspend



End Block



This patient likely has **gallstone ileus**, an uncommon complication of longstanding cholelithiasis that usually occurs in elderly women. A large (typically  $\geq 2.5$  cm) gallstone causes formation of a **cholecystoenteric fistula** between the gallbladder and adjoining gut (most often the duodenum) due to pressure necrosis and erosion of these tissues.

Fistula formation allows passage of the gallstone into the small bowel, where it travels freely until it becomes trapped in the **ileum**, the narrowest portion of the intestine. Patients consequently develop symptoms/signs of **small bowel obstruction**, including abdominal pain/distension, nausea/vomiting, high-pitched (tinkling) bowel sounds, and tenderness to palpation. Abdominal x-ray may reveal dilated loops of bowel with air-fluid levels due to intestinal obstruction. Communication between the intestine and gallbladder may also allow gas to enter the biliary tree (**pneumobilia**).

**(Choice A)** Obstruction of the common bile duct by a gallstone (choledocholithiasis) can lead to pancreatitis and/or cholangitis. Cholangitis typically presents with fever, right upper quadrant abdominal pain, and jaundice (Charcot triad). Pneumobilia and features of small bowel obstruction are not characteristic.

**(Choice B)** Obstruction of the cystic duct by a gallstone may result in biliary colic or acute cholecystitis.

Acute cholecystitis usually presents with fever, abdominal pain, leukocytosis, and an inspiratory pause.







characteristic.

**(Choice B)** Obstruction of the cystic duct by a gallstone may result in biliary colic or acute cholecystitis.

Acute cholecystitis usually presents with fever, abdominal pain, leukocytosis, and an inspiratory pause during right upper quadrant palpation (Murphy sign). Pneumobilia and features of small bowel obstruction are not characteristic.

**(Choices C and E)** The caliber of the duodenum and jejunum is typically sufficient to allow passage of larger gallstones that cause gallstone ileus.

### Educational objective:

Gallstone ileus results from passage of a large gallstone through a cholecystenteric fistula into the small bowel, where it ultimately causes obstruction at the ileum. Patients typically present with symptoms/signs of small bowel obstruction, and an abdominal x-ray may reveal gas within the gallbladder and biliary tree.

### References

- [Gallstone ileus: case report and literature review.](#)

Anatomy

Gastrointestinal & Nutrition

Cholecystitis

Subject

System

Topic





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

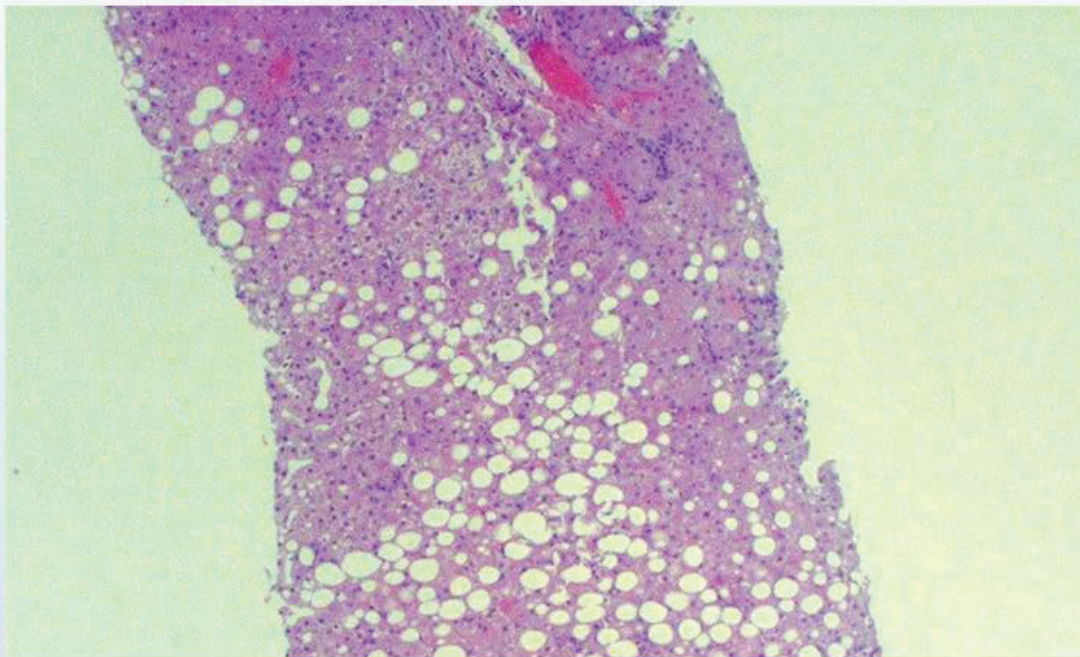


Text Zoom



Settings

A 32-year-old man with mild abdominal discomfort and anorexia admits consuming large amounts of alcohol recently. He undergoes a liver biopsy, which shows the light microscopy findings seen in the image below.



Block Time Remaining: 00:11:39

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

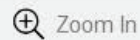
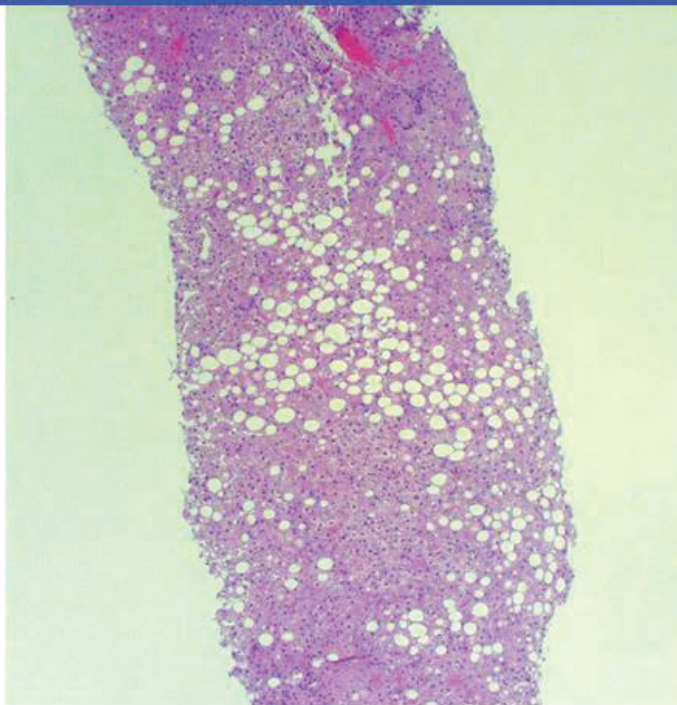


Text Zoom

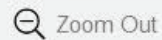


Settings

## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook

Block Time Remaining: 00:11:42

<https://t.me/USMLEWorldStep1>

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Feedback

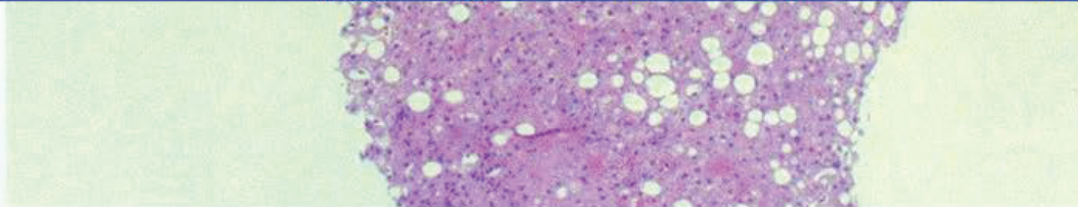
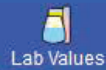


Suspend



End Block





Which of the following is the most likely cause of this patient's condition?

- ☐ A. Decreased triglyceride synthesis
- ☐ B. Decreased free fatty acid oxidation
- ☐ C. Increased phospholipid catabolism
- ☐ D. Enhanced lipoprotein assembly
- ☐ E. Increased gluconeogenesis
- ☐ F. Increased glucose uptake into cells

Submit

Block Time Remaining: 00:11:45

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



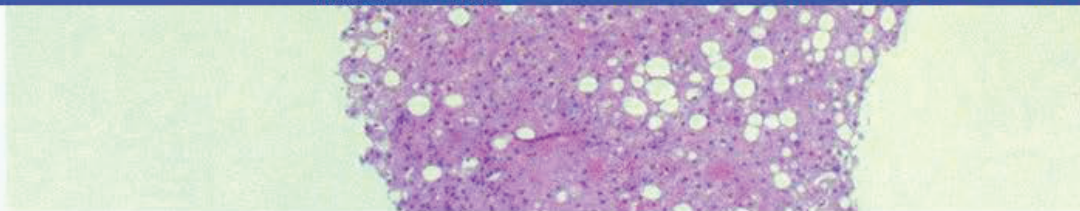
Reverse Color



Text Zoom



Settings



Which of the following is the most likely cause of this patient's condition?

- ☐ A. Decreased triglyceride synthesis (5%)
- ☒ B. Decreased free fatty acid oxidation (68%)
- ☐ C. Increased phospholipid catabolism (6%)
- ☐ D. Enhanced lipoprotein assembly (13%)
- ☒ E. Increased gluconeogenesis (3%)
- ☐ F. Increased glucose uptake into cells (2%)

Incorrect

Correct answer



68%

Answered correctly



01 min, 24 secs

Time spent



10/08/2020

Last updated

Block Time Remaining: 00:13:01

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Hepatic steatosis is a nonspecific condition characterized by triglyceride accumulation within the hepatocellular cytoplasm. The pathogenesis of alcohol-induced hepatic steatosis appears related primarily to a decrease in free fatty acid oxidation secondary to excess NADH production by the 2 major alcohol metabolism enzymes, alcohol dehydrogenase and aldehyde dehydrogenase. Contributing pathogenetic factors include impaired lipoprotein assembly and secretion and an increase in peripheral fat catabolism. As seen in the image, fatty tissue that is routinely fixed will microscopically demonstrate cytoplasmic vacuoles as the lipid is dissolved during histologic processing. In frozen sections, lipids can be demonstrated by staining with oil red O or Sudan black.

**(Choice A)** Alcohol-induced hepatic steatosis is associated with increased (not decreased) triglyceride synthesis.

**(Choice C)** Increased peripheral fat (not phospholipid) catabolism is associated with alcohol-induced hepatic steatosis.

**(Choice D)** Impaired (not enhanced) lipoprotein assembly is associated with alcohol-induced hepatic steatosis.

**(Choice E)** The alteration of the hepatic NAD/NADH ratio in alcoholics induces fatty liver through inhibition of gluconeogenesis and fatty acid oxidation.



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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Synthesis:

**(Choice C)** Increased peripheral fat (not phospholipid) catabolism is associated with alcohol-induced hepatic steatosis.

**(Choice D)** Impaired (not enhanced) lipoprotein assembly is associated with alcohol-induced hepatic steatosis.

**(Choice E)** The alteration of the hepatic NAD/NADH ratio in alcoholics induces fatty liver through inhibition of gluconeogenesis and fatty acid oxidation.

**(Choice F)** Increased glucose uptake into cells occurs when high insulin levels are circulating; this condition is not associated with hepatic steatosis.

### Educational objective:

The pathogenesis of alcohol-induced hepatic steatosis appears related primarily to a decrease in free fatty acid oxidation secondary to excess NADH production by the 2 major alcohol metabolism enzymes, alcohol dehydrogenase and aldehyde dehydrogenase.

Pathology

Subject

Gastrointestinal &amp; Nutrition

System

Alcoholic liver disease

Topic

Block Time Remaining: 00:13:01

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



A 70-year-old man comes to the office due to persistent epigastric discomfort and nausea for the past several months. He has also noticed black-colored stools on several occasions. Medical history is notable for hypertension and osteoarthritis. The patient emigrated from rural China 5 years ago to live with his daughter. He does not use tobacco, alcohol, or illicit drugs. Physical examination shows a thin male with pale mucous membranes, an enlarged left supraclavicular lymph node, and epigastric tenderness on deep palpation. Stool testing for occult blood is positive. Upper gastrointestinal endoscopy reveals a 3-cm ulceration at the gastric antrum, with a heaped-up irregular border. Biopsy from the edge of the ulcer reveals glandular structures containing intestinal-like columnar cells. Which of the following most likely predisposed this patient to his current condition?

- ☐ A. Chronic use of nonsteroidal anti-inflammatory drugs
- ☐ B. Excessive consumption of salt-preserved foods
- ☐ C. Frequent intake of high-temperature beverages
- ☐ D. Functional disruption of gastroesophageal junction
- ☐ E. Increased gastrin production from a pancreatic mass





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

for hypertension and osteoarthritis. The patient emigrated from rural China 5 years ago to live with his daughter. He does not use tobacco, alcohol, or illicit drugs. Physical examination shows a thin male with pale mucous membranes, an enlarged left supraclavicular lymph node, and epigastric tenderness on deep palpation. Stool testing for occult blood is positive. Upper gastrointestinal endoscopy reveals a 3-cm ulceration at the gastric antrum, with a heaped-up irregular border. Biopsy from the edge of the ulcer reveals glandular structures containing intestinal-like columnar cells. Which of the following most likely predisposed this patient to his current condition?

- ☐ A. Chronic use of nonsteroidal anti-inflammatory drugs (22%)
- ☒ B. Excessive consumption of salt-preserved foods (58%)
- ☐ C. Frequent intake of high-temperature beverages (5%)
- ☐ D. Functional disruption of gastroesophageal junction (4%)
- ☐ E. Increased gastrin production from a pancreatic mass (9%)

Correct



58%

Answered correctly



02 mins, 09 secs

Time Spent



11/04/2020

Last Updated

Block Time Remaining: 00:15:11

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<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



### Gastric adenocarcinoma

Risk factors	<ul style="list-style-type: none"><li>• High-salt diet</li><li>• N-nitroso-containing compounds (eg, processed meat, tobacco)</li><li>• Chronic <i>Helicobacter pylori</i> infection</li><li>• Autoimmune chronic atrophic gastritis</li><li>• Obesity</li></ul>
Clinical features	<ul style="list-style-type: none"><li>• Early satiety, weight loss</li><li>• Epigastric pain, melena</li><li>• Left supraclavicular &amp;/or umbilical lymphadenopathy</li></ul>
Gross appearance/ histopathology	<p>Intestinal type:</p> <ul style="list-style-type: none"><li>• Ulcerated mass with irregular rolled or heaped-up edges</li><li>• Glandular structures with intestinal-like columnar or cuboidal cells (similar to colon adenocarcinoma)</li></ul> <p>Diffuse:</p>



appearance/  
histopathology

(similar to colon adenocarcinoma)

Diffuse:

- Plaque-like infiltration of stomach (eg, linitis plastica)
- Signet-ring cells without glandular structures

This patient with epigastric pain, occasional melena, and left supraclavicular lymphadenopathy (ie, Virchow node) has intestinal-type **gastric adenocarcinoma**, the most common primary gastric malignancy. It is typically visualized endoscopically as an **ulcerated mass** with irregular folded or heaped-up edges. Histologically, intestinal-type gastric cancer resembles colon adenocarcinoma and is characterized by **glandular** structures containing **intestinal-like columnar** (or cuboidal) cells.

Gastric cancer occurs with the highest incidence in patients from **Eastern Asia**, Eastern Europe, and South America, possibly due to the increased consumption of **salt-preserved foods** (eg, salt-cured fish), which directly damage the gastric epithelium and potentiate the effects of carcinogens. Common carcinogens associated with gastric cancer include n-nitroso-containing compounds (eg, tobacco, processed meat) and chronic *Helicobacter pylori* infection, both of which may also be present at increased levels in these populations. Other risk factors include obesity and autoimmune atrophic gastritis.

(Choices A and E) Chronic nonsteroidal anti-inflammatory drug use and gastrin-producing tumors (ie,





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choices A and E)** Chronic nonsteroidal anti-inflammatory drug use and gastrin-producing tumors (ie, Zollinger-Ellison syndrome) are associated with benign peptic ulcer disease, not gastric adenocarcinoma. Benign ulcers are typically clean-based with regular borders (as opposed to this patient's ulcerated lesion with irregular, heaped-up borders); in addition, intestinal metaplasia is unexpected.

**(Choice C)** Excessive consumption of hot beverages is associated with esophageal squamous cell carcinoma, not gastric adenocarcinoma.

**(Choice D)** Disruption of the lower esophageal sphincter enables gastric acid to reflux into the esophagus, which predisposes patients to esophageal intestinal metaplasia (eg, Barrett esophagus) and ultimately esophageal adenocarcinoma. However, this is not a risk factor for gastric adenocarcinoma.

### Educational objective:

Intestinal-type gastric adenocarcinoma is visualized endoscopically as an ulcerated mass with irregular folded or heaped-up edges. Histologically, it resembles colon adenocarcinoma and is characterized by glandular structures containing intestinal-like columnar (or cuboidal) cells. Risk factors include *Helicobacter pylori* infection, a high-salt diet, n-nitroso-containing compounds, and autoimmune atrophic gastritis.

### References



1



Feedback

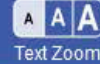
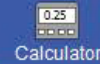
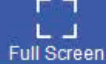


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End Block





A 5-week-old boy is brought to the emergency department after having tonic-clonic movements of his left upper and lower extremity that lasted approximately 3 minutes. The patient was born at home at 38 weeks gestation to a 23-year-old primigravida. The patient's mother received prenatal care, took prenatal vitamins, and had a healthy diet during pregnancy. The infant's newborn screen was positive for cystic fibrosis, and confirmatory testing is pending. The infant has been breastfeeding and gaining weight well. He has never taken any medications and also has received no vaccinations. On examination, the infant is postictal but no longer seizing. A head CT scan shows a right-sided intracranial hemorrhage. Which of the following is the most likely cause of this infant's presentation?

- ☐ A. Failure of amino acid hydroxylation
- ☐ B. Failure of fatty acid oxidation
- ☐ C. Failure of rhodopsin production
- ☐ D. Impaired gamma carboxylation
- ☐ E. Ineffective erythropoiesis
- ☐ F. Reduced activation of intranuclear receptors





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

upper and lower extremity that lasted approximately 3 minutes. The patient was born at home at 38 weeks gestation to a 23-year-old primigravida. The patient's mother received prenatal care, took prenatal vitamins, and had a healthy diet during pregnancy. The infant's newborn screen was positive for cystic fibrosis, and confirmatory testing is pending. The infant has been breastfeeding and gaining weight well. He has never taken any medications and also has received no vaccinations. On examination, the infant is postictal but no longer seizing. A head CT scan shows a right-sided intracranial hemorrhage. Which of the following is the most likely cause of this infant's presentation?

- ☐ A. Failure of amino acid hydroxylation (10%)
- ☐ B. Failure of fatty acid oxidation (7%)
- ☐ C. Failure of rhodopsin production (3%)
- ☒ D. Impaired gamma carboxylation (68%)
- ☐ E. Ineffective erythropoiesis (3%)
- ☐ F. Reduced activation of intranuclear receptors (6%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



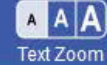
Notes



Calculator



Reverse Color



Text Zoom



Settings

### Neonatal vitamin K deficiency

<b>Etiology</b>	<ul style="list-style-type: none"><li>• Low vitamin K stores at birth (poor placental transfer, sterile gut, low content in breast milk)</li><li>• Neonatal liver cannot use vitamin K efficiently</li></ul>
<b>Presentation</b>	<ul style="list-style-type: none"><li>• Intracranial, gastrointestinal, cutaneous, umbilical &amp; surgical site <b>bleeding</b></li></ul>
<b>Prevention</b>	<ul style="list-style-type: none"><li>• Intramuscular vitamin K at birth</li></ul>

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**Vitamin K**, a **fat-soluble** vitamin, is an **essential cofactor** for gamma-glutamyl carboxylase, an enzyme that **carboxylates coagulation factors II, VII, IX, and X**.

Infants are born with low vitamin K stores due to poor transplacental transfer. Their livers are unable to use vitamin K efficiently and breast milk is low in this vitamin. Additional risk factors for neonatal vitamin K deficiency include parental **refusal of vitamin K prophylaxis** at birth and **exclusive breastfeeding**.



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Infants are born with low vitamin K stores due to poor transplacental transfer. Their livers are unable to use vitamin K efficiently and breast milk is low in this vitamin. Additional risk factors for neonatal vitamin K deficiency include parental **refusal of vitamin K prophylaxis** at birth and **exclusive breastfeeding**. Patients with **cystic fibrosis (CF)** are also at risk for vitamin K deficiency due to malabsorption of fat-soluble vitamins.

Vitamin K deficiency can result in a **life-threatening bleeding diathesis**, such as intracranial hemorrhage and profuse bleeding from the gastrointestinal tract, umbilicus, and surgical sites. Deficiency is prevented by intramuscular supplementation at birth.

**(Choice A)** Vitamin C (ascorbic acid) deficiency results in defective collagen synthesis due to failure of hydroxylation of proline and lysine. Mucosal bleeding and bruising are typical manifestations in severely malnourished individuals and those who misuse drugs or alcohol. However, breast milk provides adequate ascorbic acid.

**(Choice B)** Vitamin B3 (niacin) deficiency results in failure of formation of nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), which are required for fatty acid oxidation and synthesis, respectively. Niacin deficiency presents with pellagra (ie, dermatitis, diarrhea, and dementia).





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

acid oxidation and synthesis, respectively. Niacin deficiency presents with pellagra (ie, dermatitis, diarrhea, and dementia).

**(Choices C and F)** Patients with CF are at risk for deficiency of both vitamins A and D. Reduced activation of intranuclear receptors occurs in vitamin D deficiency, and exclusively breastfed infants require vitamin D supplementation to prevent hypocalcemia and rickets due to the low content of this vitamin in breast milk. Vitamin A deficiency impairs rhodopsin formation and leads to night blindness and xerophthalmia.

**(Choice E)** Erythropoiesis requires folate, and deficiency leads to megaloblastic anemia.

### Educational objective:

Vitamin K is necessary for the carboxylation and functionality of coagulation factors II, VII, IX, and X.

Newborns who do not receive prophylactic supplementation are at risk for bleeding complications. Patients with cystic fibrosis are also at risk for vitamin K deficiency due to poor absorption of fat-soluble vitamins.

### References

- [Rise in late onset vitamin K deficiency bleeding in young infants because of omission or refusal of prophylaxis at birth.](#)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 30-year-old man comes to the emergency department with a 4-day history of progressively worsening abdominal pain and bloody diarrhea. He was started on mesalamine therapy 6 months ago after being diagnosed with ulcerative colitis but has been noncompliant with treatment. His temperature is 38.8 C (102 F), blood pressure is 100/70 mm Hg, and pulse is 130/min. The patient is lethargic and has dry mucous membranes. There is marked abdominal distension and tenderness without rebound or guarding. Rectal examination shows guaiac-positive, maroon-colored, liquid stool. Which of the following is the best next step in this patient's workup?

- ☐ A. Abdominal ultrasonography
- ☐ B. Barium enema
- ☐ C. Colonoscopy
- ☐ D. Plain abdominal x-ray
- ☐ E. Small-bowel contrast study

**Submit**

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 30-year-old man comes to the emergency department with a 4-day history of progressively worsening abdominal pain and bloody diarrhea. He was started on mesalamine therapy 6 months ago after being diagnosed with ulcerative colitis but has been noncompliant with treatment. His temperature is 38.8 C (102 F), blood pressure is 100/70 mm Hg, and pulse is 130/min. The patient is lethargic and has dry mucous membranes. There is marked abdominal distension and tenderness without rebound or guarding. Rectal examination shows guaiac-positive, maroon-colored, liquid stool. Which of the following is the best next step in this patient's workup?

- ☐ A. Abdominal ultrasonography (10%)
- ☐ B. Barium enema (8%)
- ☒ C. Colonoscopy (42%)
- ☐ D. Plain abdominal x-ray (35%)
- ☐ E. Small-bowel contrast study (4%)

Incorrect

Block Time Remaining: 00:16:48

TUTOR

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



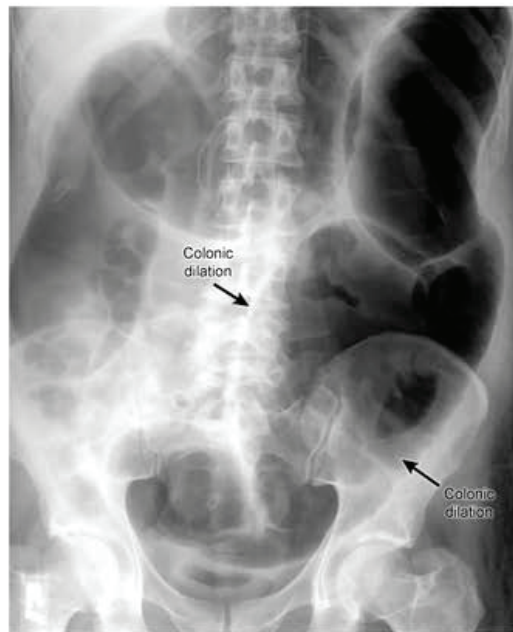
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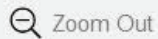
Settings

## Exhibit Display

## Toxic megacolon



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient with abdominal pain/distension, bloody diarrhea, fever, and signs of shock (eg, hypotension, tachycardia) in the setting of untreated ulcerative colitis likely has **toxic megacolon**. This is a common life-threatening complication of inflammatory bowel disease and is seen more frequently in **ulcerative colitis** than in Crohn disease. Toxic megacolon can also be associated with *Clostridium difficile* infection and other forms of infectious colitis.

Severe, occasionally transmural inflammation causes release of inflammatory mediators, bacterial products, and increased nitric oxide, which contribute to colonic smooth muscle paralysis. Rapid colonic distension ensues, thinning the intestinal wall and making it prone to perforation. Plain **abdominal x-ray** is the preferred diagnostic imaging study as it may show **colonic dilation** (as seen above) with multiple air-fluid levels (not seen in this image). Free air may also be visualized in the setting of intestinal rupture, which presents with generalized peritonitis (eg, abdominal rebound tenderness/guarding).

**(Choice A)** Abdominal ultrasonography is not typically performed to diagnose toxic megacolon. It is usually obtained in patients with acute right upper quadrant abdominal pain (eg, due to cholecystitis, ascending cholangitis) or suspected nephrolithiasis. It is also helpful in the setting of acute abdominal trauma to identify intraperitoneal free fluid.

**(Choices B and C)** Barium enema and colonoscopy are normally contraindicated in patients with







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choices B and C)** Barium enema and colonoscopy are normally contraindicated in patients with suspected toxic megacolon as these may cause perforation.

**(Choice E)** Small-bowel contrast studies can be useful in the evaluation of small-bowel obstruction (eg, abdominal pain/distension, nausea, vomiting). However, this patient's history of untreated ulcerative colitis and bloody diarrhea is more consistent with toxic megacolon, which involves the large intestine.

### Educational objective:

Toxic megacolon is a well-recognized complication of ulcerative colitis. Patients typically present with abdominal pain/distension, bloody diarrhea, fever, and signs of shock. Plain abdominal x-ray is the preferred diagnostic imaging study. Barium contrast studies and colonoscopy are contraindicated due to the risk of perforation.

### References

- [Toxic megacolon.](#)
- [A new look at toxic megacolon: an update and review of incidence, etiology, pathogenesis, and management.](#)

Pathology

Gastrointestinal &amp; Nutrition

Toxic megacolon

Block Time Remaining: 00:16:48

TUTOR

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Laparotomy performed in a 4-year-old Caucasian girl with abdominal pain reveals a blind pouch connected to the ileum. The pouch is removed; under microscopy, it demonstrates pancreatic acini in the mucosa. The latter finding would be best described as which of the following?

- ☐ A. Hypoplasia
- ☐ B. Hyperplasia
- ☒ C. Metaplasia
- ☐ D. Dysplasia
- ☐ E. Ectopy

**Submit**

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Laparotomy performed in a 4-year-old Caucasian girl with abdominal pain reveals a blind pouch connected to the ileum. The pouch is removed; under microscopy, it demonstrates pancreatic acini in the mucosa. The latter finding would be best described as which of the following?

- ☐ A. Hypoplasia (1%)
- ☐ B. Hyperplasia (1%)
- ☐ C. Metaplasia (13%)
- ☐ D. Dysplasia (3%)
- ☒ E. Ectopy (79%)

Correct



79%

Answered correctly



35 secs

Time Spent



01/30/2021

Last Updated

Explanation

Block Time Remaining: 00:17:23

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Feedback

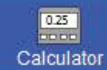


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Meckel diverticulum is the most common congenital anomaly of the small intestine, being present in 2% of the population. It forms due to incomplete obliteration of the omphalomesenteric duct that connects the midgut lumen and yolk sac cavity early in fetal life. Meckel diverticulum is connected to the ileum, and is located approximately 2 feet proximal to the ileocecal valve.

A variety of tissues have been found in Meckel diverticulum, including gastric, pancreatic, colonic, jejunal, duodenal and endometrial. The most common of these is gastric tissue, which is significant because gastric epithelium produces acid that can cause ulceration of adjacent tissues and lower GI bleeding. Meckel diverticulum most often presents with painless melena. The diverticulum may also become inflamed and simulate the clinical presentation of acute appendicitis.

Gastric, pancreatic, and other types of mucosa found in Meckel diverticulum are examples of ectopy (also called heterotopy). "Ectopy" is a term that identifies microscopically and functionally normal cells/tissues found in an abnormal location due to embryonic maldevelopment.

**(Choice A)** Hypoplasia is an embryologically-associated decrease in the number of cells resulting in decreased volume or size of the organ or tissue. Renal hypoplasia is an example of this abnormality.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice A)** Hypoplasia is an embryologically-associated decrease in the number of cells resulting in decreased volume or size of the organ or tissue. Renal hypoplasia is an example of this abnormality.

**(Choice B)** Hyperplasia is a compensatory increase in the number of cells with a subsequent increase in the size of an organ. Endometrial hyperplasia due to estrogen hypersecretion is an example of this process.

**(Choice C)** Replacement of one type of epithelium with another type not typical for location is called metaplasia. Unlike ectopia, which is the result of congenital malformation, metaplasia occurs during adult life and is initially a compensatory process. Metaplasia increases cancer risk in varying degrees.

**(Choice D)** Dysplasia includes a number of changes, such as pleomorphism, increased size of the nucleus, loss of cellular orientation, and loss of characteristics of the original tissue. Dysplasia is a sign of malignant transformation.

**Educational Objective:**

A number of ectopic tissues are found in Meckel diverticulum—most commonly, gastric epithelium. Gastric mucosa is present in 80% of cases of symptomatic Meckel diverticulum. Gastric acid production leads to ulceration and subsequent bleeding.



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 15-year-old boy comes to the office for a follow-up appointment. Since early childhood, he has suffered from recurrent respiratory infections and chronic diarrhea. The patient has been hospitalized several times for parenteral antibiotic treatment. Current prescribed medications include pancreatic enzyme therapy and a number of dietary supplements. Physical examination shows decreased proprioception and hyporeflexia in the lower extremities. Laboratory findings are suggestive of mild hemolytic anemia. Which of the following conditions is the most likely cause of these findings?

- ☐ A. Niacin deficiency
- ☐ B. Riboflavin deficiency
- ☐ C. Thiamine deficiency
- ☐ D. Vitamin A deficiency
- ☐ E. Vitamin C overuse
- ☐ F. Vitamin D deficiency
- ☐ G. Vitamin E deficiency
- ☐ H. Vitamin K deficiency



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Feedback



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End Block

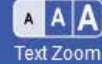
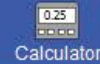
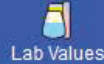
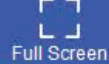




from recurrent respiratory infections and chronic diarrhea. The patient has been hospitalized several times for parenteral antibiotic treatment. Current prescribed medications include pancreatic enzyme therapy and a number of dietary supplements. Physical examination shows decreased proprioception and hyporeflexia in the lower extremities. Laboratory findings are suggestive of mild hemolytic anemia. Which of the following conditions is the most likely cause of these findings?

- ☐ A. Niacin deficiency
- ☐ B. Riboflavin deficiency
- ☐ C. Thiamine deficiency
- ☐ D. Vitamin A deficiency
- ☐ E. Vitamin C overuse
- ☐ F. Vitamin D deficiency
- ☐ G. Vitamin E deficiency
- ☐ H. Vitamin K deficiency





A 15-year-old boy comes to the office for a follow-up appointment. Since early childhood, he has suffered from recurrent respiratory infections and chronic diarrhea. The patient has been hospitalized several times for parenteral antibiotic treatment. Current prescribed medications include pancreatic enzyme therapy and a number of dietary supplements. Physical examination shows decreased proprioception and hyporeflexia in the lower extremities. Laboratory findings are suggestive of mild hemolytic anemia. Which of the following conditions is the most likely cause of these findings?

- ☐ A. Niacin deficiency
- ☐ B. Riboflavin deficiency
- ☐ C. Thiamine deficiency
- ☐ D. Vitamin A deficiency
- ☐ E. Vitamin C overuse
- ☐ F. Vitamin D deficiency
- ☐ G. Vitamin E deficiency
- ☐ H. Vitamin K deficiency





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

a number of dietary supplements. Physical examination shows decreased proprioception and hyporeflexia in the lower extremities. Laboratory findings are suggestive of mild hemolytic anemia. Which of the following conditions is the most likely cause of these findings?

- ☐ A. Niacin deficiency (7%)
- ☐ B. Riboflavin deficiency (6%)
- ☐ C. Thiamine deficiency (17%)
- ☐ D. Vitamin A deficiency (4%)
- ☐ E. Vitamin C overuse (2%)
- ☐ F. Vitamin D deficiency (2%)
- ☒ G. Vitamin E deficiency (53%)
- ☐ H. Vitamin K deficiency (6%)

Correct

53%



01 min, 29 secs



08/30/2020

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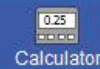
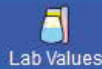


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The combination of recurrent respiratory infections and diarrhea in a child or young adult is strongly suggestive of cystic fibrosis with secondary exocrine pancreatic insufficiency. Because pancreatic enzymes are necessary for the proper absorption of nutrients in the gut, fat malabsorption with deficiencies of the fat-soluble vitamins A, D, E, and K frequently occurs in patients with cystic fibrosis.

Vitamin E primarily serves to protect fatty acids from oxidation; **vitamin E deficiency** predisposes cell membranes to oxidative injury. The cells that are most susceptible include neurons with long axons (due to large membrane surface area) and erythrocytes (due to high oxygen exposure). The most common clinical manifestations of vitamin E deficiency are **neuromuscular disease** (eg, skeletal myopathy, spinocerebellar ataxia, polyneuropathy) and **hemolytic anemia**. Involvement of the dorsal column in the spinal cord is associated with the loss of proprioception and vibratory sense. Spinocerebellar tract involvement causes ataxia, and peripheral nerve dysfunction results in hyporeflexia.

**(Choices A, B, and C)** Thiamine (vitamin B<sub>1</sub>), riboflavin (vitamin B<sub>2</sub>), and niacin (vitamin B<sub>3</sub>) are water-soluble vitamins and not affected by fat malabsorption.

**(Choice D)** Vitamin A deficiency manifests with night blindness, dry eyes (xerophthalmia), and corneal softening (keratomalacia).

**(Choice E)** Vitamin C overdose can cause nausea, abdominal pain, and diarrhea. Chronic intake of high





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choices A, B, and C)** Thiamine (vitamin B<sub>1</sub>), riboflavin (vitamin B<sub>2</sub>), and niacin (vitamin B<sub>3</sub>) are water-soluble vitamins and not affected by fat malabsorption.

**(Choice D)** Vitamin A deficiency manifests with night blindness, dry eyes (xerophthalmia), and corneal softening (keratomalacia).

**(Choice E)** Vitamin C overdose can cause nausea, abdominal pain, and diarrhea. Chronic intake of high doses of vitamin C may facilitate the development of calcium oxalate kidney stones.

**(Choice F)** Vitamin D is essential for bone formation and mineralization. Deficiency of this vitamin presents as rickets in children and as osteomalacia in adults.

**(Choice H)** Vitamin K is necessary for hepatic synthesis of clotting factors II, VII, IX, and X. Deficiency of this vitamin presents as an increased tendency to bleed.

### Educational objective:

Vitamin E deficiency can occur in individuals with fat malabsorption. Deficiency of this fat-soluble vitamin is associated with increased susceptibility of the neuronal and erythrocyte membranes to oxidative stress. Clinical manifestations include ataxia, impaired proprioception and vibratory sensation, and hemolytic anemia.

### References



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 59-year-old woman comes to the office due to fatigue and generalized itching that have developed slowly over the last year. She has not had a visible rash. The patient is reluctant to seek health care and has not seen a physician in years. She does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. Examination shows mild hepatomegaly. Laboratory studies show a striking increase in serum alkaline phosphatase, with moderate elevations in bilirubin and hepatic transaminases. Liver biopsy reveals dilated bile canaliculi with green-brown plugs and yellowish-green accumulations of pigment within the hepatic parenchyma. The patient does not return for her scheduled follow-up appointment to discuss further management. This patient is at risk for developing which of the following complications?

- ☐ A. Cardiac dilation
- ☐ B. Choreaathetosis
- ☐ C. Fat-soluble vitamin deficiency
- ☐ D. Gastric atrophy
- ☐ E. Macrocytic anemia
- ☐ F. Seborrheic dermatitis



1



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

over the last year. She has not had a visible rash. The patient is reluctant to seek health care and has not seen a physician in years. She does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. Examination shows mild hepatomegaly. Laboratory studies show a striking increase in serum alkaline phosphatase, with moderate elevations in bilirubin and hepatic transaminases. Liver biopsy reveals dilated bile canaliculi with green-brown plugs and yellowish-green accumulations of pigment within the hepatic parenchyma. The patient does not return for her scheduled follow-up appointment to discuss further management. This patient is at risk for developing which of the following complications?

- ☐ A. Cardiac dilation (3%)
- ☐ B. Choreoathetosis (8%)
- ☒ C. Fat-soluble vitamin deficiency (81%)
- ☐ D. Gastric atrophy (1%)
- ☐ E. Macrocytic anemia (3%)
- ☐ F. Seborrheic dermatitis (2%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Causes of cholestasis

<b>Intrahepatic</b>	<ul style="list-style-type: none"><li>• Drug-induced (eg, erythromycin, contraceptives)</li><li>• Primary biliary cholangitis</li><li>• Cholestasis of pregnancy</li><li>• Primary sclerosing cholangitis (may also be extrahepatic)</li></ul>
<b>Extrahepatic</b>	<ul style="list-style-type: none"><li>• Choledocholithiasis</li><li>• Malignancy (eg, pancreatic, gallbladder)</li></ul>

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This patient has fatigue, pruritus, hepatomegaly, and an elevated alkaline phosphatase level suggesting cholestatic liver disease. **Cholestasis** can arise secondary to hepatocellular dysfunction or intrahepatic or extrahepatic biliary obstruction. Both obstructive and nonobstructive cholestasis are characterized by the deposition of bile pigment within the hepatic parenchyma, often with green-brown plugs in the dilated bile canaliculi. When it is prolonged, the reduction in bile flow causes intestinal **malabsorption** of fats and **fat-soluble vitamins** (A, D, E, and K), which require bile salts for digestion.



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**soluble vitamins** (A, D, E, and K), which require bile salts for digestion.

**(Choice A)** Cardiac dilation can result from deficiency of thiamine (vitamin B<sub>1</sub>), a water-soluble vitamin.

Deficiency is common in alcoholics but not in patients with cholestatic liver disease.

**(Choice B)** Wilson disease is an autosomal recessive disorder characterized by abnormal biliary handling of copper. Liver disease with eventual cirrhosis is common. Central nervous system involvement can cause dysarthria, ataxia, and movement disorders including chorea and athetosis. Hepatocellular markers (eg, transaminases) will be elevated more prominently than cholestatic markers.

**(Choices D and E)** Atrophic gastritis can be due to autoimmune causes (pernicious anemia), *Helicobacter pylori* infection, radiation, or granulomatous conditions. Loss of intrinsic factor production by parietal cells can lead to deficiency of vitamin B<sub>12</sub> with resulting macrocytic anemia.

**(Choice F)** **Seborrheic dermatitis** is a common inflammatory condition characterized by accumulation of scaly, greasy skin on the scalp, face, ears, eyelids, and eyebrows. Severe or widespread seborrhea is seen in HIV infection and Parkinson disease, but it is not associated with cholestatic liver disease.

**Educational objective:**

Cholestatic liver disease can cause malabsorption and nutritional deficiencies of fat-soluble vitamins.



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Feedback



Suspend

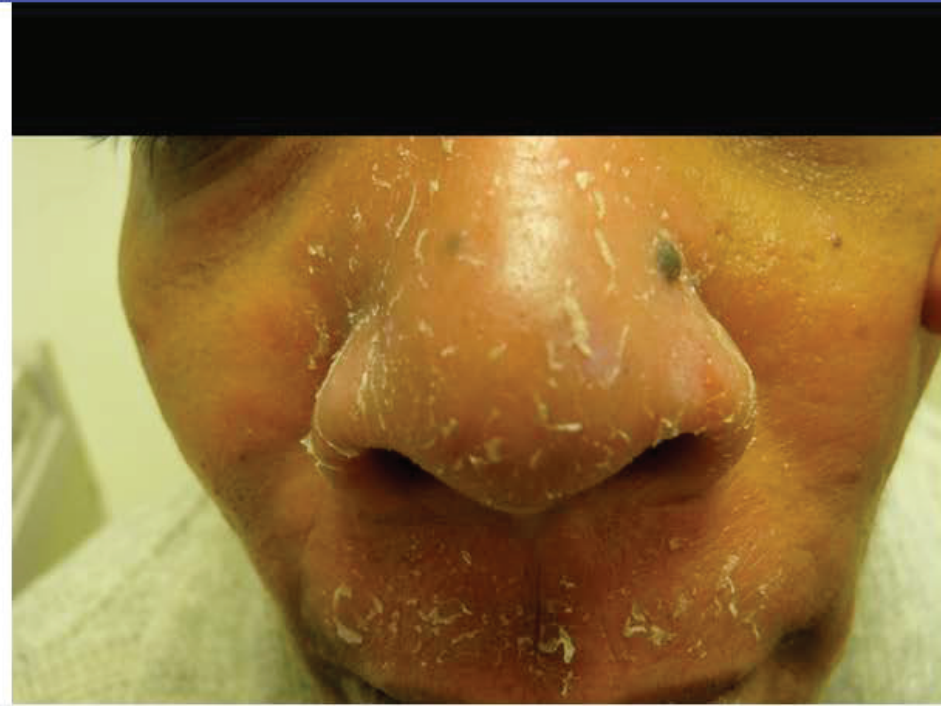


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**soluble vitamins (A, D, E, and K), which require bile salts for digestion.**

Exhibit Display



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A 26-year-old woman is evaluated for intermittent abdominal discomfort, diarrhea, and melena. The patient undergoes colonoscopy followed by total colectomy due to significant colonic abnormalities. Representative colon findings are shown in the image below.



Her sister, who has the same biological parents and has no symptoms, also undergoes screening



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Her sister, who has the same biological parents and has no symptoms, also undergoes screening colonoscopy and has similar findings. If left untreated, which of the following is the most likely lifetime risk of colon cancer in the patient's sister?

- ☐ A. About 25%
- ☐ B. About 50%
- ☐ C. About 75%
- ☒ D. Close to 100%
- ☐ E. Same as general population

**Submit**

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Feedback

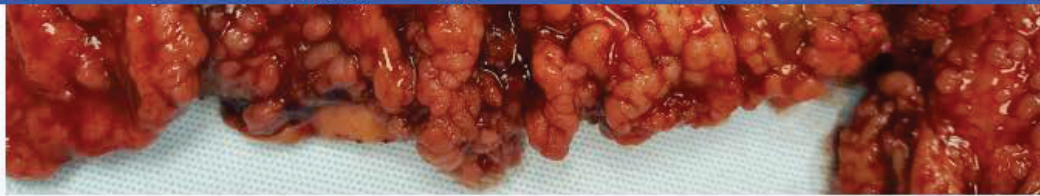


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Her sister, who has the same biological parents and has no symptoms, also undergoes screening colonoscopy and has similar findings. If left untreated, which of the following is the most likely lifetime risk of colon cancer in the patient's sister?

- ☐ A. About 25% (3%)
- ☐ B. About 50% (6%)
- ☐ C. About 75% (4%)
- ☒ D. Close to 100% (83%)
- ☐ E. Same as general population (1%)

Correct

83%

09 secs

10/06/2020

### Syndromes that increase colon cancer risk

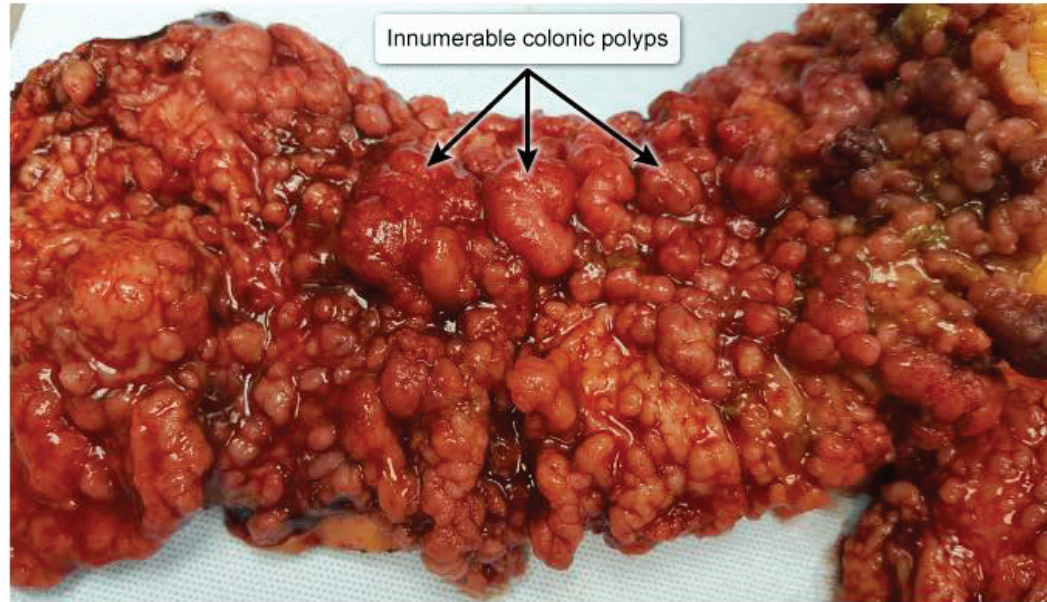
Syndrome	Gene mutation	Colon cancer risk	Other associated neoplasms
Familial adenomatous polyposis	APC	100%	Upper gastrointestinal Thyroid Desmoids/osteomas
Lynch syndrome	MSH2/6, MLH1	50%-80%	Endometrial Ovarian
Peutz-Jeghers syndrome	STK11	39%	Upper gastrointestinal Pancreatic Breast

This patient and her sister have **innumerable colonic polyps**, raising strong suspicion for the autosomal dominant hereditary disorder **familial adenomatous polyposis (FAP)**. Patients with this disorder develop

hundreds or thousands of colonic polyps in the second or third decade of life. These polyps have

Exhibit Display

Familial adenomatous polyposis



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Zoom In

Zoom Out

Reset

New | Existing

My Notebook





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient and her sister have **innumerable colonic polyps**, raising strong suspicion for the autosomal dominant hereditary disorder **familial adenomatous polyposis (FAP)**. Patients with this disorder develop hundreds or thousands of **colonic polyps** in the second or third decade of life. These polyps behave similarly to colonic polyps that form in patients who do not have FAP (spontaneous polyps): they typically grow over time, do not regress, and are associated with a progressive risk for high-grade dysplasia and transformation to invasive cancer as they enlarge. Because patients with FAP have innumerable polyps, the risk that one or more will transform into invasive **colonic carcinoma is nearly 100%**. Therefore, colectomy is generally recommended.

FAP is caused by a germline mutation to the tumor suppressor gene ***adenomatous polyposis coli (APC)***. The **APC** gene encodes for a protein that destroys beta-catenin. Loss of the APC protein results in elevated beta-catenin levels, which stimulates a transcriptional activator that leads to proliferation of intestinal crypt cells (and the subsequent formation of polyps). Patients may also have extracolonic manifestations such as gastric or duodenal polyps, desmoid tumors, and brain cancer, but these manifestations have lower penetrance than colonic polyps.

Loss of control of the APC pathway is a crucial first step in the development of both hereditary and sporadic forms of colon cancer. Nearly 80% of sporadic colon cancers have somatic mutations to both **APC** alleles;



Feedback



Suspend



End Block



intestinal crypt cells (and the subsequent formation of polyps). Patients may also have extracolonic manifestations such as gastric or duodenal polyps, desmoid tumors, and brain cancer, but these manifestations have lower penetrance than colonic polyps.

Loss of control of the APC pathway is a crucial first step in the development of both hereditary and sporadic forms of colon cancer. Nearly 80% of sporadic colon cancers have somatic mutations to both *APC* alleles; the remainder usually have activating mutations to the downstream products of this pathway.

### Educational objective:

Familial adenomatous polyposis (FAP) is an autosomal dominant disorder caused by germline mutation to the tumor suppressor gene *adenomatous polyposis coli*. Patients with FAP develop hundreds or thousands of colonic polyps; lifetime risk of colon cancer is close to 100%.

### References

- [Hereditary and familial colon cancer.](#)

Pathology

Gastrointestinal &amp; Nutrition

Colorectal polyps and cancer

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

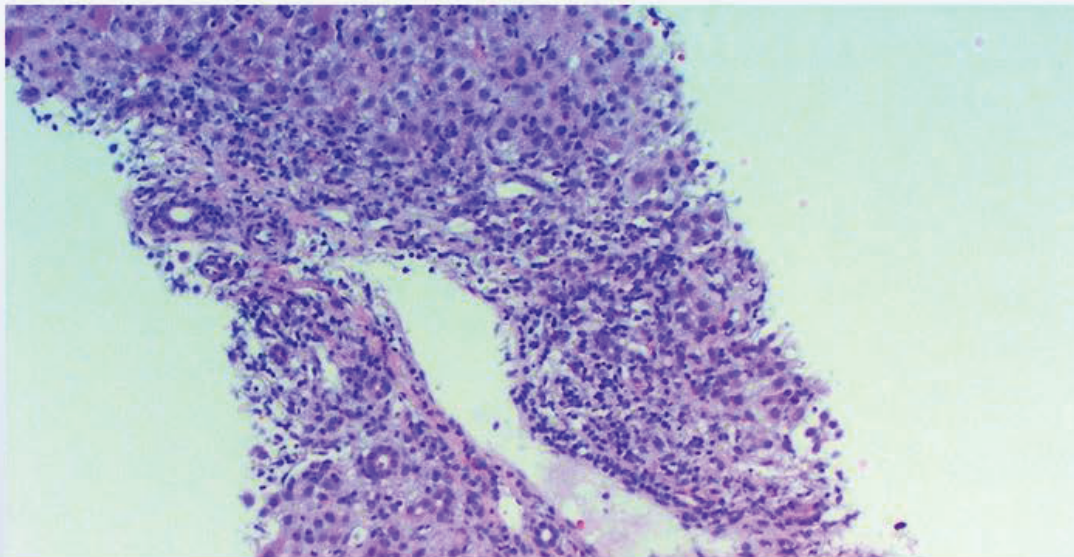


Text Zoom



Settings

A 43-year-old man is evaluated in the hospital for a medical illness. He has traveled to various countries on missionary trips and recently returned from South America. The patient has no prior medical history and takes no medications. His father has a history of alcohol dependence complicated by cirrhosis and portal hypertension. A liver biopsy is performed, and light microscopy of the tissue demonstrates spotty hepatocyte necrosis and inflammatory cell infiltration, as shown in the image below.



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

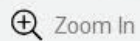
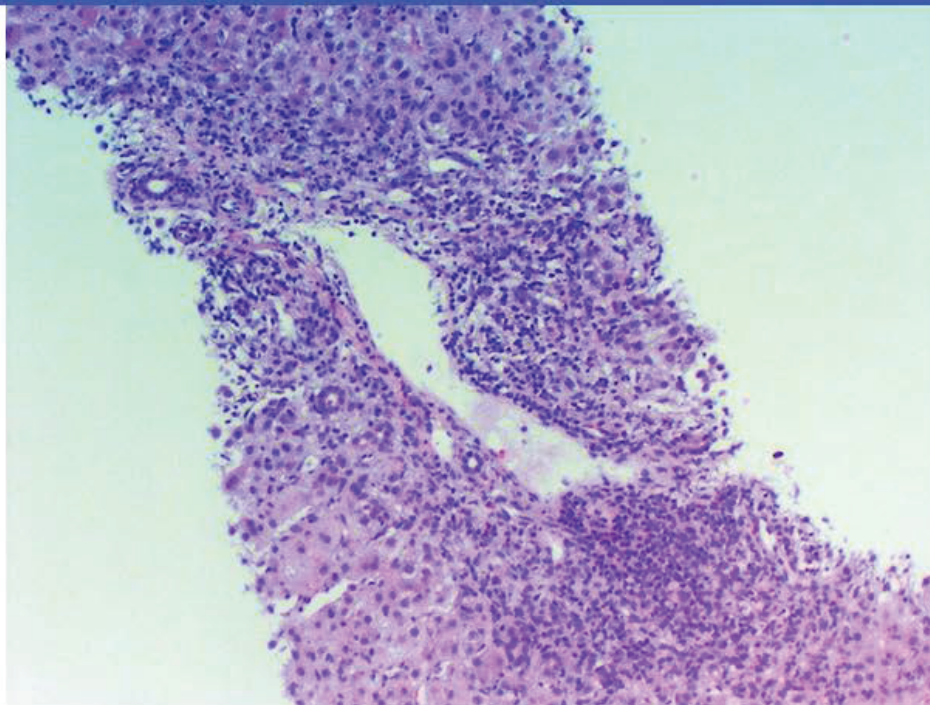


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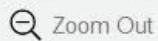


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Zoom In



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Reset



New | Existing



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0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

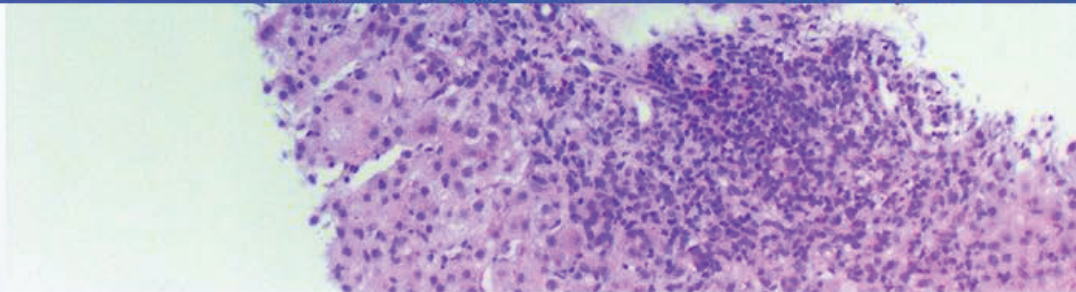
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the most likely initial clinical presentation of this patient?

- ☐ A. Clay-colored stools and osteoporosis
- ☐ B. Fever, anorexia, and dark-colored urine
- ☐ C. Prolonged pruritus and fatigue
- ☐ D. Skin pigmentation and diabetes mellitus
- ☐ E. Upper gastrointestinal bleeding and ascites

**Submit**

Block Time Remaining: 00:20:09

TUTOR

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Feedback

Suspend

End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

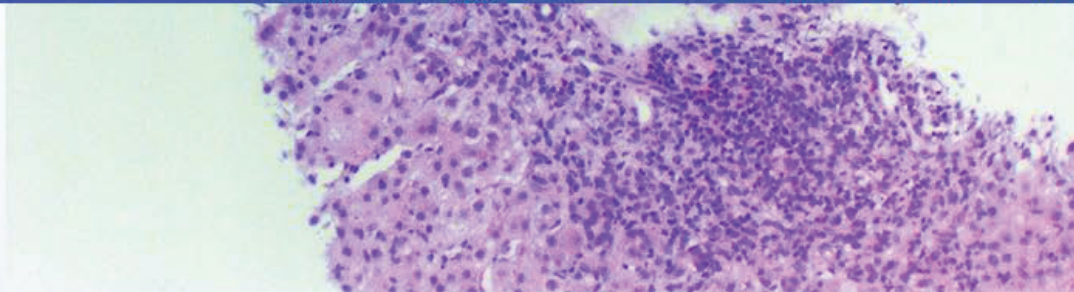
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the most likely initial clinical presentation of this patient?

- ☐ A. Clay-colored stools and osteoporosis (3%)
- ☒ B. Fever, anorexia, and dark-colored urine (62%)
- ☐ C. Prolonged pruritus and fatigue (19%)
- ☐ D. Skin pigmentation and diabetes mellitus (5%)
- ☐ E. Upper gastrointestinal bleeding and ascites (8%)

Correct

62%



01 min, 39 secs



02/01/2021

Block Time Remaining: 00:21:39

TUTOR

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Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient's liver biopsy findings and recent travel to an endemic region suggest **acute hepatitis A infection**. Acute viral hepatitis is characterized histologically by the presence of "spotty necrosis" with **ballooning degeneration** (hepatocyte swelling with wispy/clear cytoplasm), Councilman bodies (eosinophilic apoptotic hepatocytes), and **mononuclear cell infiltrates**.

Patients typically present acutely with a prodrome of **fever**, malaise, **anorexia**, nausea/vomiting, and right upper quadrant abdominal pain. After several days (up to 1 week), prodromal symptoms lessen as patients develop signs of cholestasis such as jaundice, pruritus, **dark-colored urine** (due to increased conjugated bilirubin levels), and acholic stool (lacks bilirubin pigment). The illness is self-limited and does not progress to chronic hepatitis, cirrhosis, or hepatocellular carcinoma.

**(Choices A and C)** Chronic cholestatic processes (eg, primary biliary cirrhosis, primary sclerosing cholangitis) may present initially with prolonged pruritus and fatigue. As these conditions progress, patients can develop acholic stools and malabsorption of fat-soluble vitamins (due to reduced bile flow to the small intestine). This can lead to vitamin D deficiency and metabolic bone disease (eg, osteoporosis, osteomalacia).

**(Choice D)** Skin pigmentation and diabetes mellitus are more suggestive of hemochromatosis, an inherited disease associated with iron overload in the liver, pancreas, heart, and other organs.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



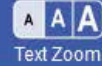
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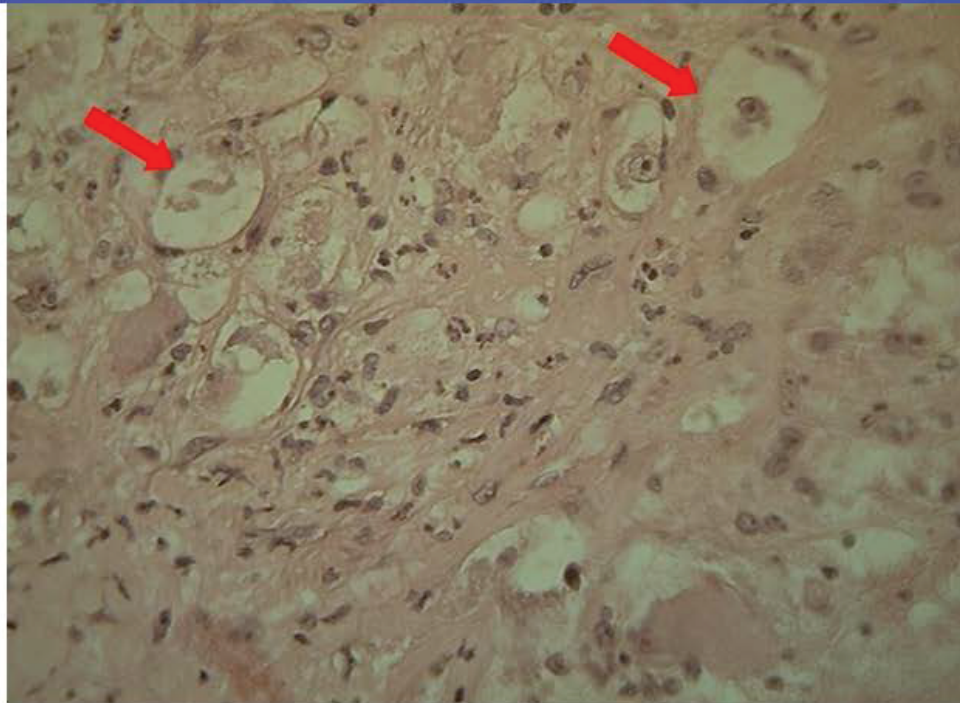


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Settings

## Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Inherited disease associated with iron overload in the liver, pancreas, heart, and other organs.

Block Time Remaining: 00:21:39

TUTOR

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0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

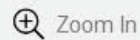
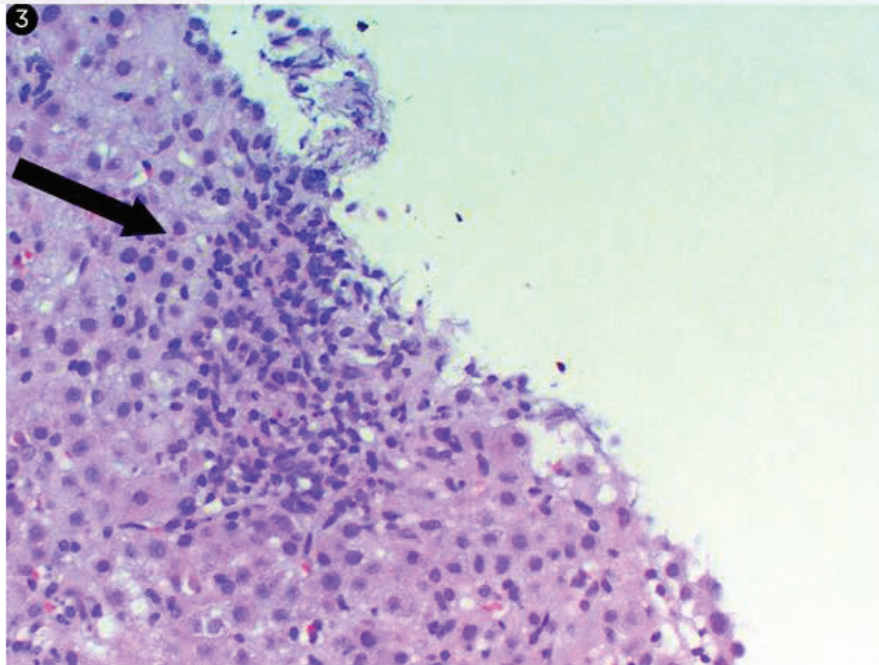


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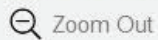


Settings

## Exhibit Display

Acute hepatitis Acute hepatitis

Zoom In



Zoom Out



Reset



New | Existing



My Notebook



0



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

can develop acholic stools and malabsorption of fat-soluble vitamins (due to reduced bile flow to the small intestine). This can lead to vitamin D deficiency and metabolic bone disease (eg, osteoporosis, osteomalacia).

**(Choice D)** Skin pigmentation and diabetes mellitus are more suggestive of hemochromatosis, an inherited disease associated with iron overload in the liver, pancreas, heart, and other organs.

**(Choice E)** Upper gastrointestinal bleeding and ascites are more suggestive of portal hypertension, a condition that typically develops secondary to liver cirrhosis.

### Educational objective:

Acute hepatitis A is a self-limited infection that typically presents acutely with prodromal symptoms (eg, fever, malaise, anorexia, nausea/vomiting, right upper quadrant pain) followed by signs of cholestasis (eg, jaundice, pruritus, dark-colored urine, clay-colored stool).

### References

- Pathology of acute hepatitis A in humans. Comparison with acute hepatitis B.
- Hepatitis A.

Pathology

Gastrointestinal &amp; Nutrition

Hepatitis a





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 44-year-old man with a history of heavy alcohol consumption comes to the emergency department with a nosebleed after getting into a fight while intoxicated. Continuous local pressure is applied and his bleeding resolves within 30 minutes. A detailed physical examination is performed after the bleeding subsides and shows distended paraumbilical veins, ascites, and a flapping hand tremor on wrist extension. Which of the following laboratory findings would be most indicative of a poor prognosis for this patient?

- ☐ A. High aspartate aminotransferase
- ☐ B. High fibrinogen levels
- ☐ C. High gamma glutamyl transferase
- ☐ D. Prolonged bleeding time
- ☐ E. Prolonged prothrombin time

**Submit**

1



Feedback



Suspend



End Block




A 44-year-old man with a history of heavy alcohol consumption comes to the emergency department with a nosebleed after getting into a fight while intoxicated. Continuous local pressure is applied and his bleeding resolves within 30 minutes. A detailed physical examination is performed after the bleeding subsides and shows distended paraumbilical veins, ascites, and a flapping hand tremor on wrist extension. Which of the following laboratory findings would be most indicative of a poor prognosis for this patient?

- ☐ A. High aspartate aminotransferase (19%)
- ☐ B. High fibrinogen levels (3%)
- ☐ C. High gamma glutamyl transferase (14%)
- ☒ D. Prolonged bleeding time (5%)
- ☒ E. Prolonged prothrombin time (56%)

Incorrect

Correct answer  
E

 56%  
Answered correctly

 36 secs  
Time Spent

 10/30/2020  
Last Updated





### Laboratory abnormalities in cirrhosis

<b>Indicators of liver function</b>	<b>Impaired biosynthetic capacity</b> <ul style="list-style-type: none"> <li>Elevated prothrombin time</li> <li>Hypoalbuminemia</li> </ul> <b>Impaired transport and metabolic capacity</b> <ul style="list-style-type: none"> <li>Elevated bilirubin</li> </ul>
<b>Indicators of liver injury</b>	<b>Markers of hepatocyte injury</b> <ul style="list-style-type: none"> <li>Elevated aspartate &amp; alanine aminotransferases (AST usually &gt;ALT)</li> </ul> <b>Markers of cholestasis</b> <ul style="list-style-type: none"> <li>Elevated alkaline phosphatase</li> <li>Elevated gamma-glutamyl transpeptidase</li> </ul>
<b>Other</b>	<ul style="list-style-type: none"> <li>Thrombocytopenia (due to splenic sequestration of platelets)</li> </ul>

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This patient has **clinical findings** consistent with alcoholic cirrhosis, namely signs of portal hypertension (ascites/caput medusa) and hepatic encephalopathy (asterixis). Alcohol-associated hepatic injury evolves through the stages of alcoholic steatosis (reversible), alcoholic hepatitis (reversible), and alcoholic cirrhosis



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient has **clinical findings** consistent with alcoholic cirrhosis, namely signs of portal hypertension (ascites/caput medusa) and hepatic encephalopathy (asterixis). Alcohol-associated hepatic injury evolves through the stages of alcoholic steatosis (reversible), alcoholic hepatitis (reversible), and alcoholic cirrhosis (irreversible).

Laboratory findings in cirrhosis reflect both hepatocellular/biliary injury and loss of hepatic function.

Hepatocyte injury causes a release of intracellular enzymes and an increase in serum transaminases; biliary injury is reflected by increases in alkaline phosphatase and gamma-glutamyl transpeptidase (GGT).

Although these laboratory studies are indicative of ongoing hepatobiliary injury, they do not provide information on the liver's functional reserve, a key determinant of prognosis in patients with cirrhosis.

Serum albumin levels and prothrombin time (PT) are better indicators of the liver's biosynthetic function, and its ability to transport and metabolize organic anions is reflected by the serum bilirubin level.

Hypoalbuminemia, elevated bilirubin levels, and prolonged PT are signs of inadequate liver function (eg, liver failure) and indicate a poor prognosis in cirrhotic patients. For this reason, they are included in multiple scoring systems used to assess the severity of liver failure and need for transplantation.

**(Choice A)** A high aspartate aminotransferase (AST) indicates hepatocellular injury and release of intracellular enzymes into the blood. AST is classically elevated to more than 2 times the level of alanine aminotransferase in alcoholic liver disease. Transaminase elevations do not reflect liver function and do







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice A)** A high aspartate aminotransferase (AST) indicates hepatocellular injury and release of intracellular enzymes into the blood. AST is classically elevated to more than 2 times the level of alanine aminotransferase in alcoholic liver disease. Transaminase elevations do not reflect liver function and do not predict outcomes; these enzymes can be transiently elevated by a number of self-limited processes.

**(Choice B)** Fibrinogen is a coagulation factor and an acute phase protein. Liver fibrinogen synthesis is increased in response to infection or acute inflammation and diminished in liver failure. Therefore, low fibrinogen levels would be expected in liver failure.

**(Choice C)** When the alkaline phosphatase is elevated, serum GGT measurements can differentiate whether the cause is biliary disease or an alternate cause such as bone disease. GGT elevations are more specific for biliary injury.

**(Choice D)** The bleeding time is a measure of platelet function (not liver synthetic function) and is often prolonged in severe alcoholic liver disease, although with a fair degree of variance. Thrombocytopenia in alcoholism develops due to both direct toxic effects of alcohol on the bone marrow and hypersplenism with splenic sequestration of platelets.

**Educational objective:**

Increased aspartate aminotransferase and alanine aminotransferase are indicators of hepatocellular



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

fibrinogen levels would be expected in liver failure.

**(Choice C)** When the alkaline phosphatase is elevated, serum GGT measurements can differentiate whether the cause is biliary disease or an alternate cause such as bone disease. GGT elevations are more specific for biliary injury.

**(Choice D)** The bleeding time is a measure of platelet function (not liver synthetic function) and is often prolonged in severe alcoholic liver disease, although with a fair degree of variance. Thrombocytopenia in alcoholism develops due to both direct toxic effects of alcohol on the bone marrow and hypersplenism with splenic sequestration of platelets.

### Educational objective:

Increased aspartate aminotransferase and alanine aminotransferase are indicators of hepatocellular damage, and increased alkaline phosphatase and gamma-glutamyl transpeptidase indicate biliary injury. Serum albumin levels, bilirubin levels, and prothrombin time are reflective of liver function and are of greatest prognostic significance in patients with cirrhosis.

Pathology

Gastrointestinal &amp; Nutrition

Cirrhosis

Subject

System

Topic



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 25-year-old man comes to the hospital due to worsening abdominal pain, distension, and nausea and vomiting for 3 days. He has a 4-year history of recurrent abdominal pain associated with diarrhea, low-grade fever, and easy fatigability. The symptoms usually occur after stress and resolve spontaneously in a few days. However, this time, the patient's symptoms persisted and worsened. He has no other medical problems and takes no medications on a regular basis. Temperature is 38.2 C (100.8 F), blood pressure is 110/70 mm Hg, pulse is 104/min, and respirations are 16/min. BMI is 19 kg/m<sup>2</sup>. Examination shows a tender mass in the right lower quadrant of the abdomen. Imaging is consistent with small-bowel obstruction. Laparotomy reveals that the abdominal mass is composed of inflamed small bowel, adherent and indurated mesentery, and enlarged abdominal lymph nodes. The affected region of the small bowel is resected. Which of the following is most likely to be seen on histologic examination of this patient's intestine?

- ☐ A. Caseating granulomas in all layers of the intestine
- ☒ B. Flask-shaped ulcers with narrow necks and broad bases
- ☐ C. Inflammation limited to the mucosa and submucosa
- ☐ D. Pseudomembranes of fibrin and inflammatory debris



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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- ☐ A. Caseating granulomas in all layers of the intestine
- ☐ B. Flask-shaped ulcers with narrow necks and broad bases
- ☐ C. Inflammation limited to the mucosa and submucosa
- ☐ D. Pseudomembranes of fibrin and inflammatory debris
- ☐ E. Thickening of the muscularis mucosae

**Submit**

Block Time Remaining: 00:22:20

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Feedback



Suspend



End Block





problems and takes no medications on a regular basis. Temperature is 38.2 C (100.8 F), blood pressure is 110/70 mm Hg, pulse is 104/min, and respirations are 16/min. BMI is 19 kg/m<sup>2</sup>. Examination shows a tender mass in the right lower quadrant of the abdomen. Imaging is consistent with small-bowel obstruction. Laparotomy reveals that the abdominal mass is composed of inflamed small bowel, adherent and indurated mesentery, and enlarged abdominal lymph nodes. The affected region of the small bowel is resected. Which of the following is most likely to be seen on histologic examination of this patient's intestine?

- ☐ A. Caseating granulomas in all layers of the intestine (45%)
- ☐ B. Flask-shaped ulcers with narrow necks and broad bases (11%)
- ☐ C. Inflammation limited to the mucosa and submucosa (17%)
- ☐ D. Pseudomembranes of fibrin and inflammatory debris (8%)
- ☒ E. Thickening of the muscularis mucosae (17%)

Correct

17%



01 min, 10 secs



09/25/2020

Block Time Remaining: 00:23:25

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



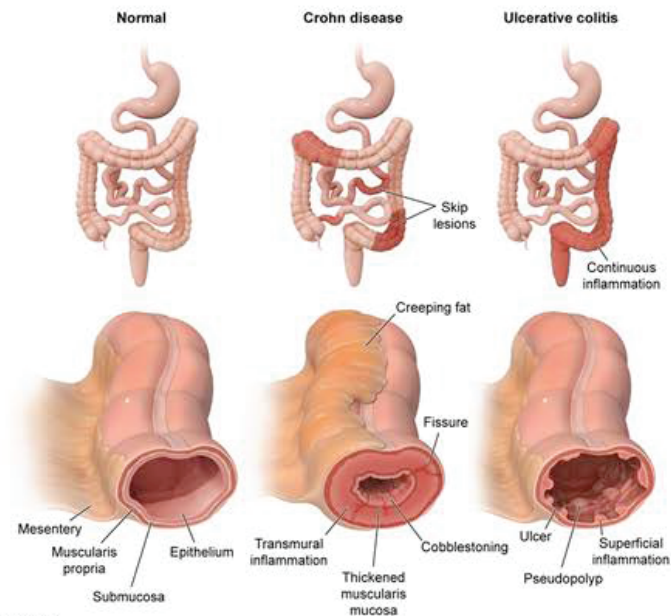
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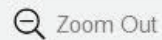
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## Exhibit Display

## Crohn disease vs ulcerative colitis



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Reset



New

Existing



My Notebook



1



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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This patient with recurrent abdominal pain and diarrhea likely has **Crohn disease** (CD) complicated by small-bowel obstruction. CD is an inflammatory bowel disease that occurs most commonly in young adults. It typically presents as recurrent episodes of abdominal pain associated with diarrhea, low-grade fevers, and fatigue; symptoms may worsen during periods of stress. The inflammation can affect any part of the gastrointestinal tract from the mouth to the anus and is typically patchy with interspersed areas of normal bowel (skip lesions). CD is characterized by **transmural inflammation** (all layers of the bowel wall are involved), which predisposes to several complications:

- **Strictures** occur as a result of bowel wall edema, fibrosis, and **hypertrophy (thickening)** of the **muscularis mucosae**, which narrows the intestinal lumen. This can progress to **bowel obstruction**.
- Fistulas occur when ulcers penetrate the entire thickness of the intestinal wall, leading to a sinus tract that communicates between multiple organs (eg, enterovesicular, enterovaginal, enteroenteric).
- **Abscesses** form when sinus tracts become walled off. They can also perforate, leading to diffuse peritonitis.

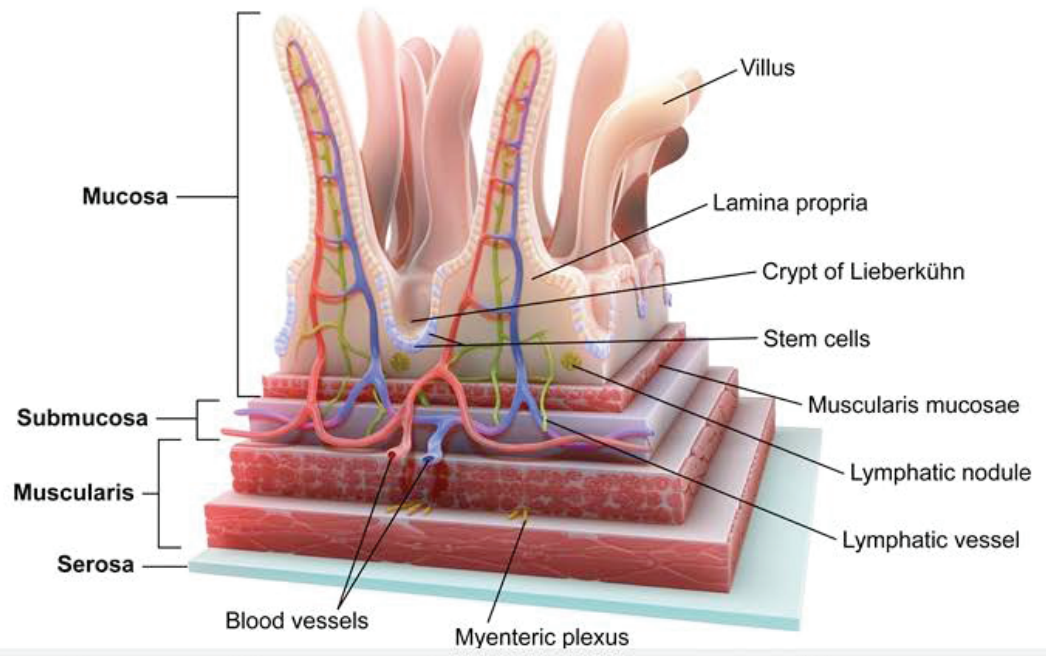
**(Choice A)** Caseating granulomas are typically seen in multiple infectious processes, most notably tuberculosis (TB). Abdominal TB can present with abdominal pain, fevers, and occasional obstruction;





### Exhibit Display

#### Small Intestinal Histology



Zoom In Zoom Out Reset New Existing My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



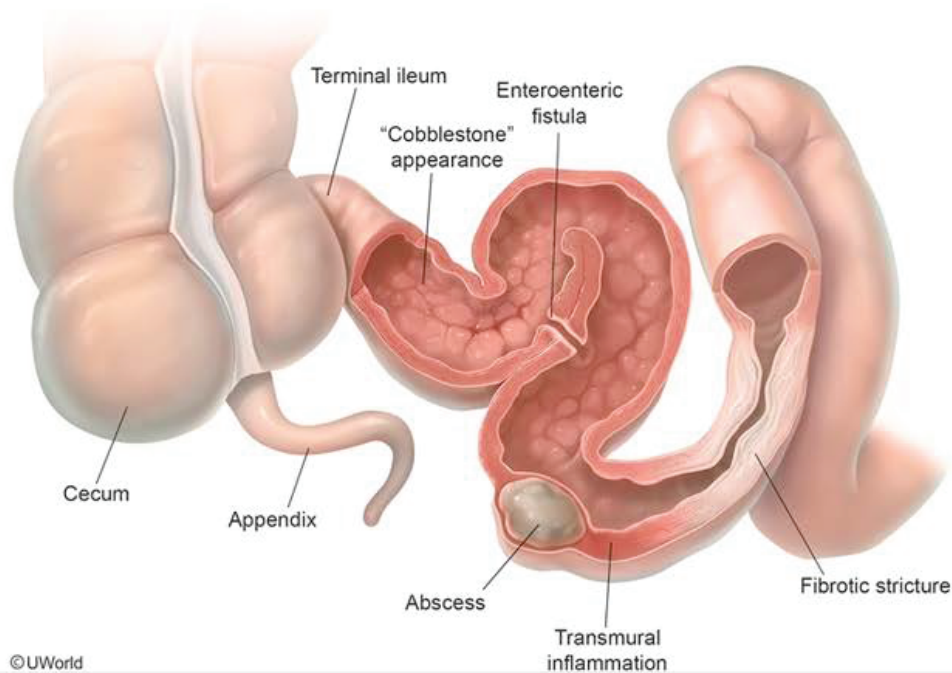
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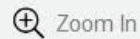
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## Exhibit Display

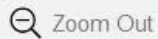
## Crohn disease



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Existing



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My Notebook



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

peritonitis.

**(Choice A)** Caseating granulomas are typically seen in multiple infectious processes, most notably tuberculosis (TB). Abdominal TB can present with abdominal pain, fevers, and occasional obstruction; however, symptoms are unlikely to spontaneously wax and wane, and evidence of TB is often present in other sites (eg, hemoptysis with pulmonary TB). CD is associated with noncaseating, rather than caseating, granulomas.

**(Choice B)** Flask-shaped ulcers in the cecum and colon are seen in *Entamoeba histolytica* infection, which occurs more commonly in developing countries and presents with bloody diarrhea. Severe cases can cause fulminant colitis with bowel necrosis, but obstruction is uncommon.

**(Choice C)** Ulcerative colitis is an inflammatory bowel disease that involves only the mucosa and submucosa. Inflammation involves contiguous areas of the colon only, and the small bowel is not involved. Due to the superficial nature of the inflammation, strictures and fistulas are not seen.

**(Choice D)** **Pseudomembranes** composed of fibrin and inflammatory debris are seen with *Clostridium difficile* infection, which is typically associated with antibiotic use. Complications include toxic megacolon; however, *C difficile* does not cause obstruction and the small bowel is not typically involved.

**Educational objective:**



1



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice B)** Flask-shaped ulcers in the cecum and colon are seen in *Entamoeba histolytica* infection, which occurs more commonly in developing countries and presents with bloody diarrhea. Severe cases can cause fulminant colitis with bowel necrosis, but obstruction is uncommon.

**(Choice C)** Ulcerative colitis is an inflammatory bowel disease that involves only the mucosa and submucosa. Inflammation involves contiguous areas of the colon only, and the small bowel is not involved. Due to the superficial nature of the inflammation, strictures and fistulas are not seen.

**(Choice D)** **Pseudomembranes** composed of fibrin and inflammatory debris are seen with *Clostridium difficile* infection, which is typically associated with antibiotic use. Complications include toxic megacolon; however, *C difficile* does not cause obstruction and the small bowel is not typically involved.

### Educational objective:

Crohn disease is characterized by patchy, transmural inflammation of the gastrointestinal tract. It can affect any part of the tract from the mouth to the anus. Complications include strictures (due to bowel wall edema, fibrosis, and thickening of the muscularis mucosae), fistulas (due to penetration of ulcers through the intestinal wall), and abscesses.

Pathology

Gastrointestinal &amp; Nutrition

Inflammatory bowel disease

Subject

System

Topic

Block Time Remaining: 00:23:25

TUTOR

<https://t.me/USMLEWorldStep1>

1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

An 8-month-old boy is brought to clinic due to abdominal distension. The patient has had excessive straining and irritability with bowel movements since birth. He had been exclusively breastfed, and his symptoms worsened after transitioning to pureed foods. Vital signs are normal. Abdominal examination shows distension with mild tenderness to palpation. Bowel sounds are present, and there is no hepatosplenomegaly. Barium enema shows a relatively narrow rectum and rectosigmoid area. The rest of the colon proximal to this segment is significantly dilated. Colorectal biopsy of which of the following areas is most likely to reveal the underlying cause of this patient's condition?

- ☐ A. Mucosa of the dilated segment
- ☐ B. Mucosa of the narrow segment
- ☐ C. Muscular layer of the dilated segment
- ☒ D. Submucosa of the dilated segment
- ☐ E. Submucosa of the narrow segment

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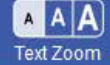
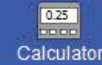
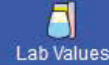
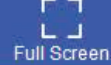
Feedback



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An 8-month-old boy is brought to clinic due to abdominal distension. The patient has had excessive straining and irritability with bowel movements since birth. He had been exclusively breastfed, and his symptoms worsened after transitioning to pureed foods. Vital signs are normal. Abdominal examination shows distension with mild tenderness to palpation. Bowel sounds are present, and there is no hepatosplenomegaly. Barium enema shows a relatively narrow rectum and rectosigmoid area. The rest of the colon proximal to this segment is significantly dilated. Colorectal biopsy of which of the following areas is most likely to reveal the underlying cause of this patient's condition?

- ☐ A. Mucosa of the dilated segment (1%)
- ☐ B. Mucosa of the narrow segment (8%)
- ☐ C. Muscular layer of the dilated segment (11%)
- ☐ D. Submucosa of the dilated segment (8%)
- ☒ E. Submucosa of the narrow segment (70%)







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Hirschsprung disease

#### Pathophysiology

- Failure of neural crest cell migration caudally to distal colon
- Absent parasympathetic ganglia in affected submucosal & myenteric plexus
- Chronically contracted colonic segment

#### Clinical features

- Delayed passage of meconium in neonates
- Chronic constipation
- Abdominal distension

#### Evaluation

- Contrast enema: narrow rectosigmoid area with dilated proximal colon
- Rectal suction biopsy (diagnostic): absent submucosal ganglia

This infant with chronic constipation and abdominal distension has barium enema findings suggestive of **Hirschsprung disease (HD)**. HD is a congenital disorder in which **neural crest cells** fail to migrate to the bowel wall during embryogenesis. These cells normally develop into ganglion cells of the **submucosal (Meissner) and myenteric (Auerbach) plexus**. In HD, the affected colon lacks parasympathetic ganglia and is therefore unable to relax. Because the neural crest cells migrate caudally along the bowel, the



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

bowel wall during embryogenesis. These cells normally develop into ganglion cells of the **submucosal**

**(Meissner) and myenteric (Auerbach) plexus**. In HD, the affected colon lacks parasympathetic ganglia and is therefore unable to relax. Because the neural crest cells migrate caudally along the bowel, the **rectosigmoid area** is most commonly involved.

Typical presentation is in the neonatal period with delayed passage of meconium and signs of bowel obstruction (eg, bilious emesis, abdominal distension). However, disease severity correlates with the length of nonfunctional bowel. Therefore, those with a short aganglionic segment may go undiagnosed with chronic, refractory **constipation** for months or years, as in this case. Characteristic findings on **contrast enema** include a narrowed rectosigmoid area (due to chronic contraction) and a dilated bowel proximal to the obstruction.

Rectal suction biopsy is the gold standard for the diagnosis of HD and should include the **submucosa** of the rectum (ie, **narrowed segment**), which is the most superficial layer that demonstrates the **absence of ganglion cells** (ie, submucosal plexus). Absence of ganglia between the longitudinal and circular layers of the muscularis externa (ie, myenteric plexus) can also be seen on full-thickness biopsies.

### Educational objective:

Absence of the submucosal (Meissner) and myenteric (Auerbach) plexuses in Hirschsprung disease causes the affected rectosigmoid region to become narrowed. The submucosa of the narrowed area is the



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



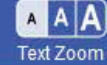
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Calculator



Reverse Color



Text Zoom



Settings

length of nonfunctional bowel. Therefore, those with a short aganglionic segment may go undiagnosed with chronic, refractory **constipation** for months or years, as in this case. Characteristic findings on **contrast enema** include a narrowed rectosigmoid area (due to chronic contraction) and a dilated bowel proximal to the obstruction.

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### Educational objective:

Absence of the submucosal (Meissner) and myenteric (Auerbach) plexuses in Hirschsprung disease causes the affected rectosigmoid region to become narrowed. The submucosa of the narrowed area is the most superficial layer where the absence of ganglion cells can be confirmed during biopsy procedures.

Pathology

Gastrointestinal &amp; Nutrition

Hirschsprung's disease

Subject

System

Topic

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1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

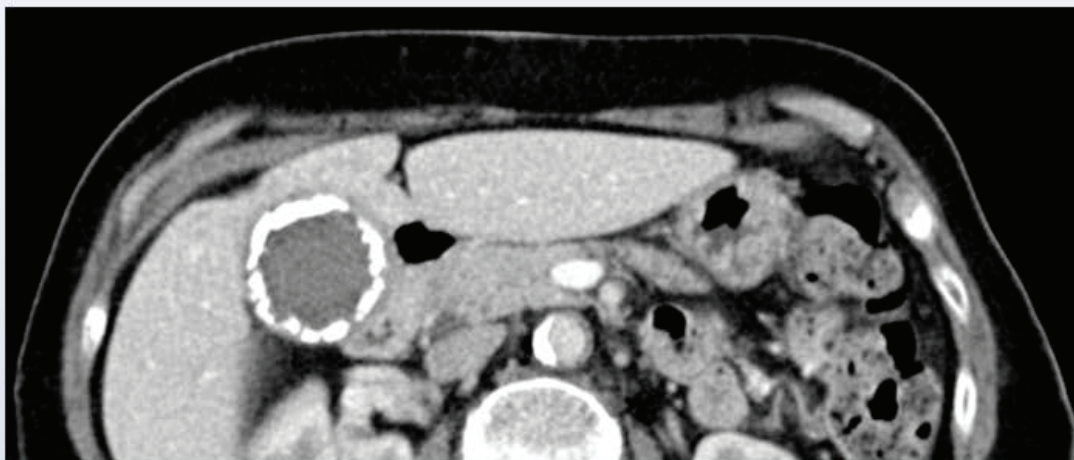


Text Zoom



Settings

A 68-year-old woman comes to the office for a preventive visit. The patient feels well, and recently lost 4 kg (8.8 lb) on a new diet and exercise regimen. She has no recent history of abdominal pain, jaundice, or changes in her stools. Past medical history is notable for hypertension and hypercholesterolemia, for which the patient takes appropriate medications. She does not use tobacco, alcohol, or illicit drugs. Vital signs are normal. On examination, the abdomen is soft and nontender, and no hepatosplenomegaly is noted. However, a firm mass is palpated in the right upper quadrant. CT scan of the abdomen is ordered and is shown below.



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

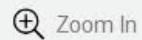


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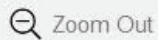


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## Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



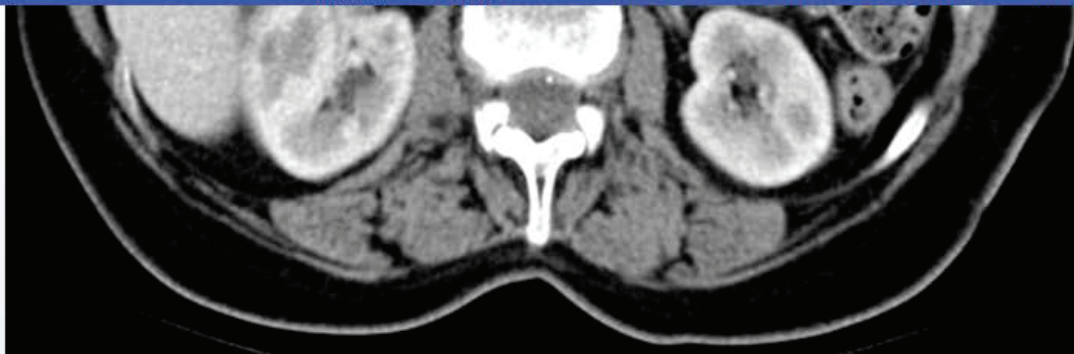
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Text Zoom



Settings



This patient is at elevated risk for which of the following conditions?

- ☐ A. Ascending cholangitis
- ☐ B. Cholangiocarcinoma
- ☐ C. Gallbladder adenocarcinoma
- ☐ D. Hepatocellular carcinoma
- ☒ E. Liver cirrhosis



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



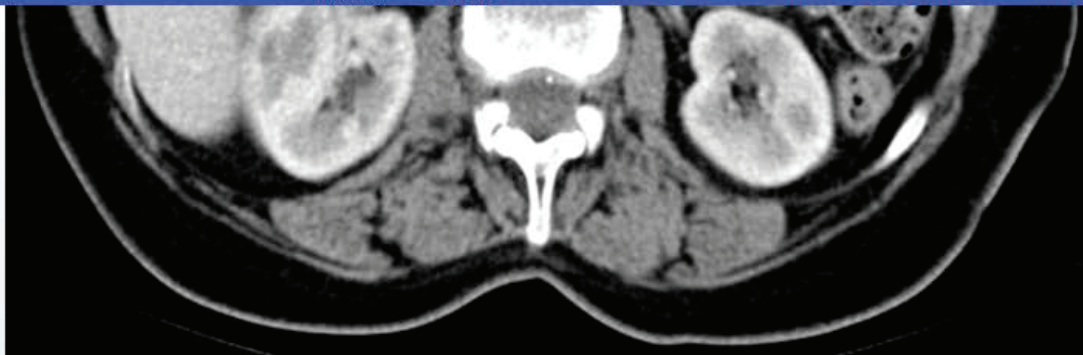
Reverse Color



Text Zoom



Settings



This patient is at elevated risk for which of the following conditions?

- ☐ A. Ascending cholangitis (13%)
- ☐ B. Cholangiocarcinoma (24%)
- ☒ C. Gallbladder adenocarcinoma (47%)
- ☐ D. Hepatocellular carcinoma (11%)
- ☐ E. Liver cirrhosis (2%)



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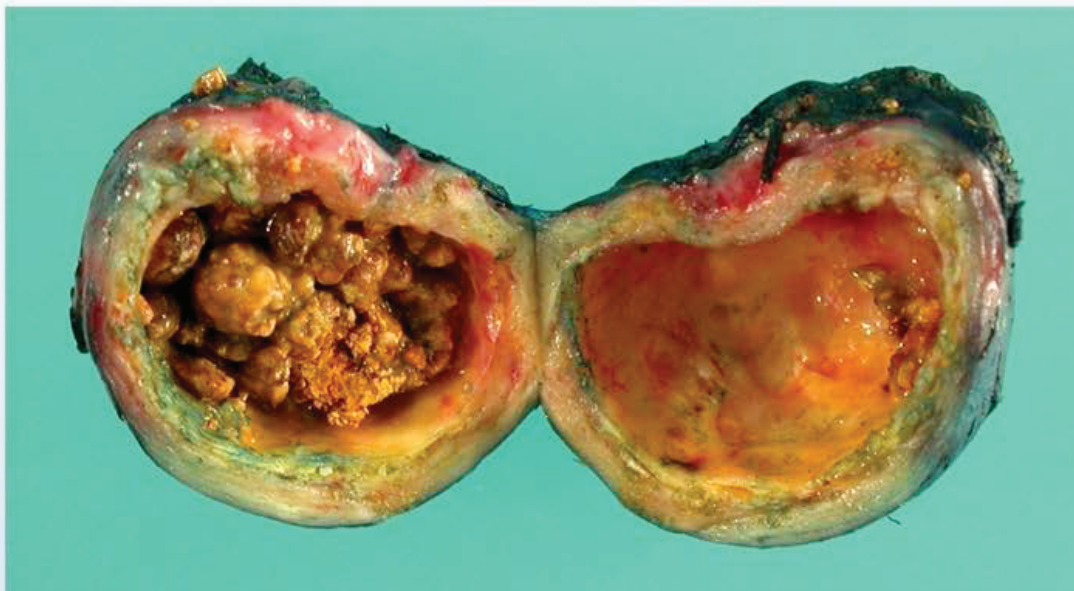
Feedback



Suspend



End Block



This patient, with a firm, palpable gallbladder and extensive calcification throughout the gallbladder wall, has typical findings of **porcelain gallbladder**. Patients with this condition may present with right upper quadrant abdominal pain but many are asymptomatic, with findings detected incidentally on imaging done



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient, with a firm, palpable gallbladder and extensive calcification throughout the gallbladder wall, has typical findings of **porcelain gallbladder**. Patients with this condition may present with right upper quadrant abdominal pain but many are asymptomatic, with findings detected incidentally on imaging done for other reasons. Radiographic features may include a **thickened gallbladder wall** with a rim of patchy or uniform **calcification**.

Porcelain gallbladder is a potential manifestation of **chronic cholecystitis** and is often found in association with multiple gallstones. The pathogenesis is due to dystrophic intramural deposition of calcium salts in the setting of chronic inflammation. Gross findings include a bluish, brittle, thickened gallbladder wall with a "crunchy" texture. Microscopic findings can include calcified plaques within the muscularis or spotty calcification in the mucosa. Porcelain gallbladder is associated with an increased risk of **adenocarcinoma of the gallbladder**.

**(Choice A)** Acute ascending cholangitis is typically due to gram-negative infection of the intrahepatic biliary tree. It is a consequence of biliary obstruction (eg, choledocholithiasis) and presents with fever, right upper quadrant abdominal pain, and jaundice.

**(Choice B)** The risk of cholangiocarcinoma is increased in fibrotic diseases of the bile ducts, such as



1



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

biliary tree. It is a consequence of biliary obstruction (eg, choledocholithiasis) and presents with fever, right upper quadrant abdominal pain, and jaundice.

**(Choice B)** The risk of cholangiocarcinoma is increased in fibrotic diseases of the bile ducts, such as primary sclerosing cholangitis, congenital fibropolycystic diseases, and chronic infection with *Opisthorchis sinensis* (liver fluke).

**(Choices D and E)** The risk of hepatocellular carcinoma is increased in many chronic inflammatory diseases of the liver, especially those progressing to cirrhosis. Common conditions include chronic viral hepatitis and alcoholic liver disease.

### Educational objective:

Porcelain gallbladder is a potential manifestation of chronic cholecystitis and is often found in association with multiple gallstones. It is due to dystrophic intramural deposition of calcium salts in the setting of chronic inflammation. Porcelain gallbladder is associated with an increased risk of adenocarcinoma of the gallbladder.

Pathology

Gastrointestinal &amp; Nutrition

Porcelain gallbladder

Subject

System

Topic

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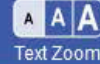
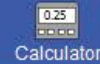
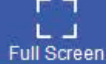
Feedback



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A 46-year-old woman comes to the emergency department due to 3 days of persistent upper abdominal pain, nausea, and vomiting. The patient has had similar pain in the past, especially after fatty meals, which resolved spontaneously within several hours. Temperature is 38.6 C (101.5 F), blood pressure is 110/65 mm Hg, and pulse is 98/min. BMI is 33 kg/m<sup>2</sup>. Physical examination is notable for severe right upper quadrant tenderness. Leukocyte count is 21,000/mm<sup>3</sup>. Laparoscopic surgery is performed and reveals an erythematous, distended gallbladder with patchy necrosis. Which of the following events most likely initiated this patient's condition?

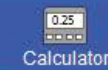
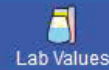
- ☐ A. Bacterial invasion of the gallbladder wall
- ☐ B. Cystic artery thrombosis
- ☐ C. Gallbladder outflow obstruction
- ☐ D. Ischemic disruption of the mucosal layer
- ☐ E. Lecithin hydrolysis and mucosal damage

**Submit**

Block Time Remaining: 00:25:55

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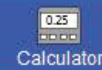
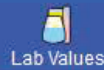


A 46-year-old woman comes to the emergency department due to 3 days of persistent upper abdominal pain, nausea, and vomiting. The patient has had similar pain in the past, especially after fatty meals, which resolved spontaneously within several hours. Temperature is 38.6 C (101.5 F), blood pressure is 110/65 mm Hg, and pulse is 98/min. BMI is 33 kg/m<sup>2</sup>. Physical examination is notable for severe right upper quadrant tenderness. Leukocyte count is 21,000/mm<sup>3</sup>. Laparoscopic surgery is performed and reveals an erythematous, distended gallbladder with patchy necrosis. Which of the following events most likely initiated this patient's condition?

- ☐ A. Bacterial invasion of the gallbladder wall (11%)
- ☐ B. Cystic artery thrombosis (1%)
- ☒ C. Gallbladder outflow obstruction (81%)
- ☐ D. Ischemic disruption of the mucosal layer (4%)
- ☐ E. Lecithin hydrolysis and mucosal damage (1%)







This patient likely has **acute calculous cholecystitis**, an acute inflammation of the gallbladder initiated by **gallstone obstruction** of the **cystic duct**. Patients typically present with persistent right upper quadrant pain, fever, and leukocytosis. Examination classically shows Murphy sign, an inspiratory pause elicited by pain during deep palpation of the right upper quadrant. Symptoms are often preceded by transient episodes of abdominal pain and nausea after fatty meals due to temporary cystic duct obstruction (biliary colic).

Persistent gallbladder outflow obstruction promotes hydrolysis of luminal lecithins to lysolecithins, which disrupts the protective mucus layer. The luminal epithelium is then exposed to the detergent action of the bile salts, resulting in chemical irritation and prostaglandin release. Inflammation of the mucosa and deeper tissues causes gallbladder hypomotility. The increasing distension and internal pressure within the gallbladder eventually result in ischemia. Finally, bacteria (eg, *Escherichia coli*, *Enterococcus*, *Klebsiella*, *Enterobacter*) invade the injured and necrotic gallbladder wall, causing an infection (**Choice A**).

(**Choices B and D**) The gallbladder is vulnerable to ischemic injury as the cystic artery lacks collateral circulation. Although inflammation/edema of the gallbladder may compromise blood flow, ischemic disruption of the mucosal layer is usually the next to last step in the pathogenesis of acute calculous cholecystitis. Gallbladder ischemia is not typically caused by cystic artery thrombosis.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

*Enterobacter*) invade the injured and necrotic gallbladder wall, causing an infection **(Choice A)**.

**(Choices B and D)** The gallbladder is vulnerable to ischemic injury as the cystic artery lacks collateral circulation. Although inflammation/edema of the gallbladder may compromise blood flow, ischemic disruption of the mucosal layer is usually the next to last step in the pathogenesis of acute calculous cholecystitis. Gallbladder ischemia is not typically caused by cystic artery thrombosis.

**(Choice E)** Lecithin hydrolysis and mucosal damage occur after gallbladder outflow obstruction in the pathogenesis of acute calculous cholecystitis.

### Educational objective:

Acute calculous cholecystitis is an acute inflammation of the gallbladder initiated by gallstone obstruction of the cystic duct. Subsequent steps in pathogenesis include mucosal disruption by lysolecithins, bile salt irritation of the luminal epithelium, prostaglandin release with transmural inflammation, gallbladder hypomotility, increased intraluminal pressure causing ischemia, and bacterial invasion.

### References

- [Acute cholecystitis.](#)

Pathology

Gastrointestinal &amp; Nutrition

Cholecystitis

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TUTOR

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

A 33-year-old woman with a 9-year history of ulcerative colitis comes to the office due to concern about her risk of colon cancer. One of her close family friends died recently from this cancer. The patient wants to "undergo all the tests for colon cancer." She has no other comorbid conditions and is under the care of a gastroenterologist who has kept her disease well controlled with sulfasalazine. Compared with sporadic colorectal carcinoma, colorectal malignancy arising in this patient would more likely exhibit which of the following features?

- ☐ A. Early *APC* gene mutation
- ☐ B. Low-grade histology
- ☐ C. Multifocal origin
- ☐ D. Origin from an adenomatous polyp

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



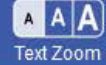
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Reverse Color



Text Zoom



Settings

A 33-year-old woman with a 9-year history of ulcerative colitis comes to the office due to concern about her risk of colon cancer. One of her close family friends died recently from this cancer. The patient wants to "undergo all the tests for colon cancer." She has no other comorbid conditions and is under the care of a gastroenterologist who has kept her disease well controlled with sulfasalazine. Compared with sporadic colorectal carcinoma, colorectal malignancy arising in this patient would more likely exhibit which of the following features?

- ☐ A. Early APC gene mutation (24%)
- ☐ B. Low-grade histology (14%)
- ☒ C. Multifocal origin (48%)
- ☐ D. Origin from an adenomatous polyp (12%)

Correct

 48%  
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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Colitis-associated vs sporadic colorectal cancer

	Colitis-associated	Sporadic
<b>Age</b>	• Younger (age 40-55)	• Older (age >60)
<b>Origin of dysplasia</b>	• Flat (nonpolypoid) lesions	• Polypoid lesions
<b>Location</b>	• Proximal > distal (particularly with CD)	• Distal > proximal
<b>Tumors</b>	• Multifocal	• Singular
<b>Histology</b>	• Mucinous and/or signet ring cells • Poorly differentiated	• Rarely mucinous • Well differentiated
<b>Mutations</b>	• Early <i>p53</i> mutation • Late <i>APC</i> gene mutation	• Early <i>APC</i> gene mutation • Late <i>p53</i> mutation

*APC* = adenomatous polyposis coli; **CD** = Crohn disease.



1



Feedback



Suspend



End Block



Previous

Next

Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Inflammatory bowel disease (IBD) is associated with a significant risk for colorectal carcinoma (CRC); up to 30% of patients with IBD develop CRC in their lifetime. Patients with ulcerative colitis, particularly pancolitis, are at highest risk. **Colitis-associated colorectal cancer** (CA-CRC) occurs in areas of chronic inflammation, and the risk is proportionate to the duration and severity of inflammation.

**(Choices A, B, and D)** Unlike sporadic CRC, which typically progresses slowly from a singular dysplastic polyp, CA-CRC is typically more **aggressive**, often evolves from flat (**nonpolypoid**) lesions, and is frequently **multifocal** (ie, multiple synchronous carcinomas) at diagnosis. CA-CRC often affects a **younger** population than sporadic CRC. These malignancies are more likely to have a **higher histopathologic grade**, with poorly differentiated or anaplastic cells and a high number of mucinous or signet ring cells. The molecular pathogenesis of CA-CRC is also different than that of sporadic disease, with *p53* mutations occurring early in the course of malignant development and *APC* mutations occurring much later.

Given the high risk for CRC and the difficulty of colonoscopic visualization of flat or multifocal lesions, it is important to regularly monitor IBD via colonoscopy with random biopsies.

**Educational objective:**



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

polyp, CA-CRC is typically more **aggressive**, often evolves from flat (**nonpolypoid**) lesions, and is frequently **multifocal** (ie, multiple synchronous carcinomas) at diagnosis. CA-CRC often affects a **younger** population than sporadic CRC. These malignancies are more likely to have a **higher histopathologic grade**, with poorly differentiated or anaplastic cells and a high number of mucinous or signet ring cells. The molecular pathogenesis of CA-CRC is also different than that of sporadic disease, with *p53* mutations occurring early in the course of malignant development and *APC* mutations occurring much later.

Given the high risk for CRC and the difficulty of colonoscopic visualization of flat or multifocal lesions, it is important to regularly monitor IBD via colonoscopy with random biopsies.

### Educational objective:

Inflammatory bowel disease, especially ulcerative pancolitis, is associated with a significant risk for colorectal carcinoma. Compared with sporadic colorectal cancer, colitis-associated colorectal cancer is more likely to occur at a younger age, is typically more aggressive with a higher histopathologic grade, often evolves from flat (nonpolypoid) lesions, and is frequently multifocal. Patients should be monitored regularly via colonoscopy with random biopsies.

### References



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

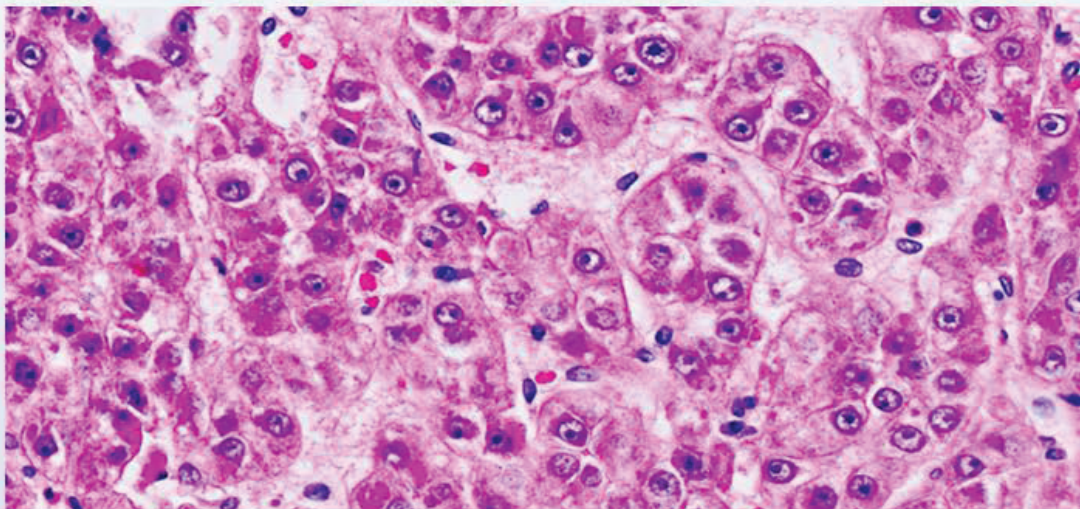


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Settings

A 58-year-old man with a history of chronic liver disease secondary to hepatitis C infection comes to the office due to progressive fatigue and abdominal discomfort. He has no other medical conditions, and a recent colonoscopy was normal. Physical examination shows ascites and jaundice. Ultrasonography of the abdomen reveals a solid mass within the liver parenchyma. Surgical resection of the liver lesion is performed. Microscopy reveals large cells with prominent nucleoli arranged in thickened plates as shown below.



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

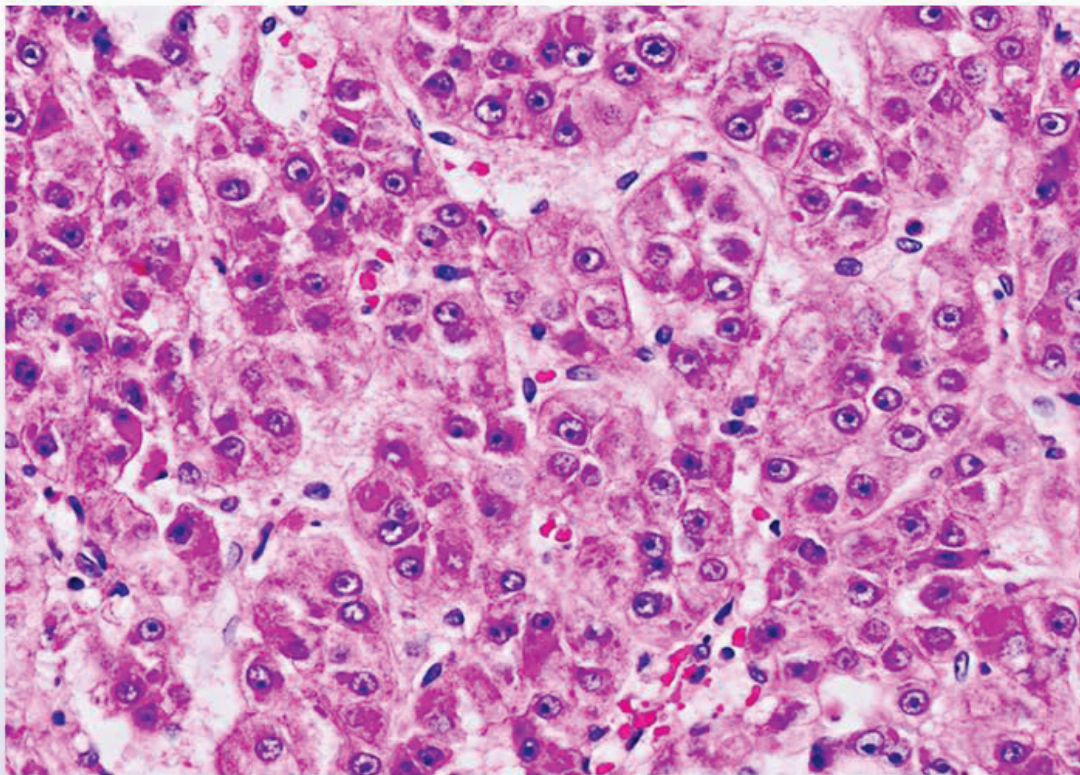


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Settings

below.



Which of the following serum markers would be most useful for monitoring this patient for disease

Block Time Remaining: 00:27:41

TUTOR

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1



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

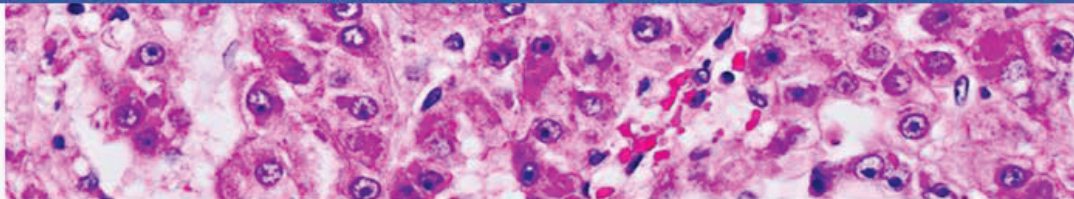
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Calculator

Reverse Color

Text Zoom

Settings



Which of the following serum markers would be most useful for monitoring this patient for disease recurrence?

- ☐ A. 5-Hydroxyindoleacetic acid
- ☐ B. Alpha-fetoprotein
- ☐ C. CA 125
- ☐ D. CA 19-9
- ☐ E. Carcinoembryonic antigen
- ☐ F. Human chorionic gonadotropin

**Submit**

Block Time Remaining: 00:27:43

TUTOR

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

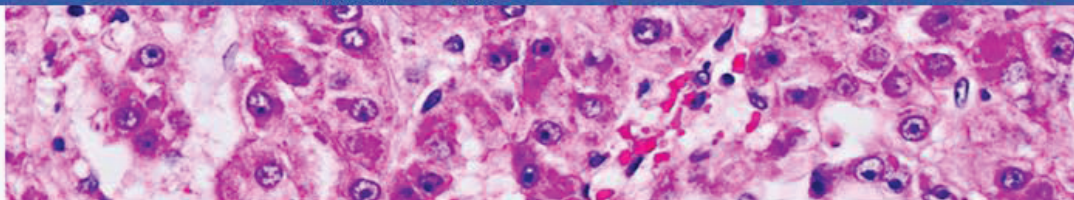
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Calculator

Reverse Color

Text Zoom

Settings



Which of the following serum markers would be most useful for monitoring this patient for disease recurrence?

- ☐ A. 5-Hydroxyindoleacetic acid (5%)
- ☒ B. Alpha-fetoprotein (67%)
- ☐ C. CA 125 (6%)
- ☐ D. CA 19-9 (7%)
- ☐ E. Carcinoembryonic antigen (12%)
- ☐ F. Human chorionic gonadotropin (0%)



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**Common serum tumor markers**

Marker	Tumor associations
<b>Alpha-fetoprotein</b>	<ul style="list-style-type: none"><li>• Hepatocellular carcinoma</li><li>• Germ cell</li></ul>
<b>CA 19-9</b>	<ul style="list-style-type: none"><li>• Pancreatic</li></ul>
<b>CA 125</b>	<ul style="list-style-type: none"><li>• Ovarian</li></ul>
<b>Carcinoembryonic antigen</b>	<ul style="list-style-type: none"><li>• Gastrointestinal (eg, colorectal)</li></ul>
<b>Human chorionic gonadotropin</b>	<ul style="list-style-type: none"><li>• Choriocarcinoma</li><li>• Germ cell</li></ul>
<b>Prostate-specific antigen</b>	<ul style="list-style-type: none"><li>• Prostate</li></ul>

**Hepatocellular carcinoma (HCC)** occurs in up to 25% of patients with chronic **hepatitis C virus (HCV)**.



1



Feedback



Suspend



End Block





**Hepatocellular carcinoma** (HCC) occurs in up to 25% of patients with chronic **hepatitis C virus** (HCV).

HCV increases hepatocyte turnover and generates local proinflammatory cytokines, which causes hepatocyte damage and fibrosis. Over time, damaged hepatocytes can proliferate into dysplastic nodules and undergo malignant transformation into HCC.

Suspicion for HCC is often raised when patients with chronic HCV develop **worsened underlying cirrhotic symptoms** such as fatigue, ascites, variceal bleeding, abdominal discomfort, or jaundice.

Abdominal imaging will show a liver mass; biopsy usually reveals abnormal thickened plates, solid sheets, or gland-like structures of **malignant hepatocytes** with a variable degree of cytologic atypia (eg, pleomorphism, high nuclear-to-cytoplasmic ratio).

Serum **alpha-fetoprotein** (AFP) level is often used to aid diagnosis and screen for disease recurrence following treatment. AFP is a glycoprotein produced by the fetal liver and yolk sac during gestation.

Although levels of AFP are often mildly or moderately elevated in patients with chronic liver disease, dramatic elevations or **sudden rises** in AFP should prompt an investigation for HCC. AFP levels do not correlate with the size or stage of the tumor and are not elevated in all cases of HCC.

**(Choice A)** 5-Hydroxyindoleacetic acid is the major breakdown product of serotonin. Elevated urine levels are seen in carcinoid tumors and certain neuroendocrine tumors.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** 5-Hydroxyindoleacetic acid is the major breakdown product of serotonin. Elevated urine levels are seen in carcinoid tumors and certain neuroendocrine tumors.

**(Choice C)** CA 125 is a serum marker associated with ovarian cancer. It may also be elevated in other malignancies (eg, endometrial) and certain benign conditions (eg, endometriosis).

**(Choice D)** CA 19-9 is primarily used as a marker for pancreatic cancer or other tumors of the biliary tract.

**(Choice E)** Carcinoembryonic antigen is a serum marker that is primarily used to monitor response to treatment in patients with colorectal cancer. This patient's clinical features (ie, chronic hepatitis C, negative colonoscopy) are consistent with HCC rather than colorectal cancer.

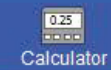
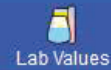
**(Choice F)** Human chorionic gonadotropin is elevated in choriocarcinoma and may also be elevated in germ cell tumors (eg, testicular). However, it is most commonly used as a marker for pregnancy.

**Educational objective:**

Alpha-fetoprotein is a serum tumor marker that is often moderately elevated in patients with chronic viral hepatitis. However, it can be strikingly elevated in those with hepatocellular carcinoma, and a sudden rise can be a sign that a patient with chronic liver disease is harboring hepatocellular carcinoma.







A 54-year-old man comes to the office due to several months of heartburn, acid regurgitation, and dysphagia. He has taken antacids and over-the-counter medications without relief. Medical history includes hypertension and hyperlipidemia. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. BMI is 32 kg/m<sup>2</sup>. Physical examination is unremarkable. Upright chest x-ray shows an opacity with an air-fluid level behind the heart. A subsequent barium swallow reveals the proximal stomach herniating through the esophageal hiatus. Which of the following pathophysiological changes most likely contributed to this patient's current condition?

- ☐ A. Cephalad migration of the squamocolumnar junction with a fixed gastroesophageal junction
- ☐ B. Circumferential laxity of the phrenoesophageal membrane
- ☐ C. Diaphragmatic muscle paralysis due to C3-5 motor nerve injury
- ☐ D. Failure of the posterolateral diaphragmatic foramina to fuse
- ☐ E. Herniation of abdominal contents through the omental foramen

**Submit**

Block Time Remaining: 00:28:10

TUTOR

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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A 54-year-old man comes to the office due to several months of heartburn, acid regurgitation, and dysphagia. He has taken antacids and over-the-counter medications without relief. Medical history includes hypertension and hyperlipidemia. The patient does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. BMI is 32 kg/m<sup>2</sup>. Physical examination is unremarkable. Upright chest x-ray shows an opacity with an air-fluid level behind the heart. A subsequent barium swallow reveals the proximal stomach herniating through the esophageal hiatus. Which of the following pathophysiological changes most likely contributed to this patient's current condition?

- ☐ A. Cephalad migration of the squamocolumnar junction with a fixed gastroesophageal junction (20%)
- ☒ B. Circumferential laxity of the phrenoesophageal membrane (59%)
- ☐ C. Diaphragmatic muscle paralysis due to C3-5 motor nerve injury (1%)
- ☐ D. Failure of the posterolateral diaphragmatic foramina to fuse (9%)
- ☐ E. Herniation of abdominal contents through the omental foramen (8%)



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Feedback



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Previous



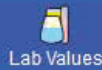
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Full Screen



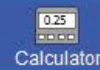
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Lab Values



Notes



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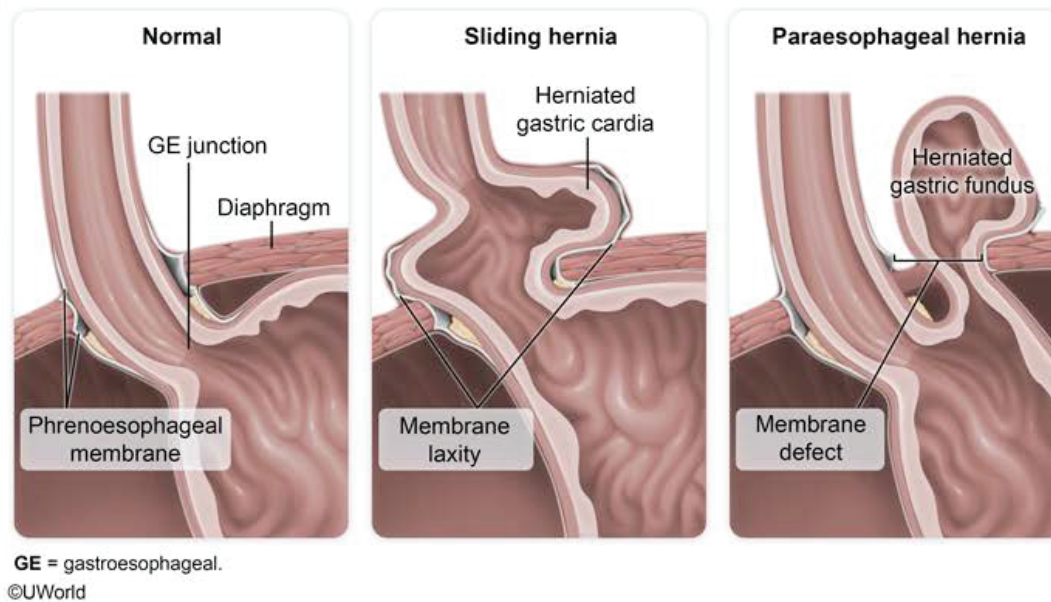


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## Hiatal hernia



This patient has a **hiatal hernia**, a common disorder in which the contents of the abdominal cavity herniate through the diaphragm into the thoracic cavity at the esophageal hiatus. The distal esophagus is normally attached circumferentially to the diaphragm by the **phrenoesophageal membrane** at the



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This patient has a **hiatal hernia**, a common disorder in which the contents of the abdominal cavity herniate through the diaphragm into the thoracic cavity at the esophageal hiatus. The distal esophagus is normally attached circumferentially to the diaphragm by the **phrenoesophageal membrane** at the gastroesophageal (GE) junction; disruptions in membrane integrity can result in hernia formation:

- **Sliding** hiatal hernias are the most common form and occur due to **laxity** of the phrenoesophageal membrane, which typically results from repetitive stress on the membrane (eg, coughing, vomiting). This allows the **GE junction** and **proximal stomach** to slide upward into the thoracic cavity and predisposes patients to reflux symptoms (eg, heartburn, regurgitation, epigastric/chest pain) due to incompetence of the lower esophageal sphincter.
- **Paraesophageal** hernias are rarer and occur due to a **defect** (hole) in the phrenoesophageal membrane. Laxity of the gastrocolic and gastrosplenic ligaments (which anchor the stomach in the abdomen) allows the **gastric fundus** to migrate into the thoracic cavity. Larger defects can also result in the subsequent herniation of the GE junction and surrounding structures (eg, bowel, spleen) into the chest. This predisposes patients to gastric volvulus, ulcerations, and respiratory complications (due to lung compression).

**(Choice A)** Barrett esophagus is the metaplastic replacement of normal squamous cells in the distal esophagus with squamocolumnar cells and occurs as a result of chronic acid reflux. Patients with Barrett







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

lung compression).

**(Choice A)** Barrett esophagus is the metaplastic replacement of normal squamous cells in the distal esophagus with squamocolumnar cells and occurs as a result of chronic acid reflux. Patients with Barrett esophagus are at increased risk of esophageal cancer, but it does not cause herniation.

**(Choice C)** Diaphragmatic muscle paralysis due to C3-5 motor nerve injury causes an elevated hemidiaphragm. Patients are typically asymptomatic (due to compensation by the other respiratory muscles), but dyspnea or orthopnea can occur. It is not associated with herniation of intrabdominal contents into the chest.

**(Choice D)** Failure of the posterolateral diaphragmatic foramina to fuse can cause a Bochdalek hernia. This congenital hernia is typically diagnosed pre- or perinatally; pulmonary hypoplasia with neonatal respiratory distress is common.

**(Choice E)** Herniation of the viscera through the omental foramen (foramen of Winslow) causes an intraabdominal hernia known as lesser sac hernia. Lesser sac hernias are very rare, typically involve the small bowel, and cause severe abdominal pain due to bowel strangulation or obstruction.

**Educational objective:**

Hiatal hernias occur when contents of the abdominal cavity herniate through the diaphragm at the



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

muscles), but dyspnea or orthopnea can occur. It is not associated with herniation of intrabdominal contents into the chest.

**(Choice D)** Failure of the posterolateral diaphragmatic foramina to fuse can cause a Bochdalek hernia. This congenital hernia is typically diagnosed pre- or perinatally; pulmonary hypoplasia with neonatal respiratory distress is common.

**(Choice E)** Herniation of the viscera through the omental foramen (foramen of Winslow) causes an intraabdominal hernia known as lesser sac hernia. Lesser sac hernias are very rare, typically involve the small bowel, and cause severe abdominal pain due to bowel strangulation or obstruction.

**Educational objective:**

Hiatal hernias occur when contents of the abdominal cavity herniate through the diaphragm at the esophageal hiatus into the thoracic cavity. Sliding hiatal hernias occur due to laxity of the phrenoesophageal membrane, leading to herniation of the gastroesophageal junction and proximal stomach, whereas paraesophageal hernias occur due to defects in the membrane, resulting in the gastric fundus herniation.

Anatomy

Gastrointestinal &amp; Nutrition

Hiatal hernia





A 53-year-old man comes to the physician due to weight loss, fatigue, and anorexia. He reports no dietary changes but has lost 6.8 kg (15 lb) in the past 2 months. Endoscopy shows an early invasive gastric cancer. The patient undergoes an uncomplicated total gastrectomy without any postoperative complications. The physician counsels the patient that he must receive lifelong administration of which of the following substances?

- ☐ A. A water-soluble vitamin
- ☐ B. Gastric enzymes
- ☐ C. Hydrochloric acid
- ☐ D. Hydrolyzed protein
- ☐ E. Medium-chain triglycerides

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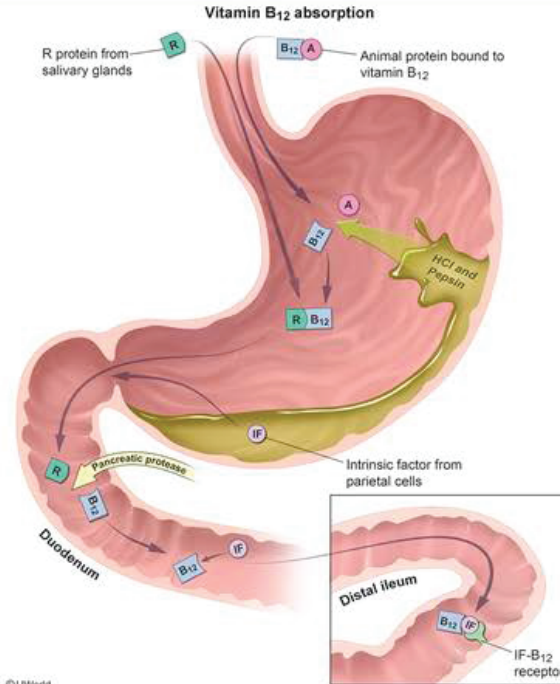
A 53-year-old man comes to the physician due to weight loss, fatigue, and anorexia. He reports no dietary changes but has lost 6.8 kg (15 lb) in the past 2 months. Endoscopy shows an early invasive gastric cancer. The patient undergoes an uncomplicated total gastrectomy without any postoperative complications. The physician counsels the patient that he must receive lifelong administration of which of the following substances?

- ☒ A. A water-soluble vitamin (68%)
- ☐ B. Gastric enzymes (15%)
- ☐ C. Hydrochloric acid (4%)
- ☐ D. Hydrolyzed protein (9%)
- ☐ E. Medium-chain triglycerides (2%)

Correct

 68%  
Answered correctly 30 secs  
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### Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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receptor

The stomach performs a number of important functions:

1. **Protein digestion** – Gastric **parietal cells** and **chief cells** produce hydrochloric acid (HCl) and pepsinogen, respectively. HCl helps to denature dietary protein (improving proteolysis) and also converts pepsinogen to its active form, **pepsin**, which preferentially cleaves polypeptides at aromatic amino acid locations. Pancreatic and intestinal proteases further degrade dietary proteins into basic amino acids in the small intestine.
2. **Intrinsic factor (IF) secretion** – Parietal cells in the body and fundus of the stomach also secrete IF, a glycoprotein that normally binds to vitamin B<sub>12</sub>. The **B<sub>12</sub>-IF complex** is then absorbed by enterocytes in the **terminal ileum**. However, in patients who have undergone total gastrectomy, IF can no longer be produced and vitamin B<sub>12</sub> cannot be effectively absorbed. Therefore, very high-dose oral or **parenteral vitamin B<sub>12</sub>** becomes necessary.
3. **Gastric reservoir** – The stomach also serves as a reservoir for ingested food. This function is lost after total gastrectomy, and accelerated emptying of hyperosmolar food boluses into the small bowel results in **dumping syndrome** (characterized by colicky abdominal pain, nausea, and diarrhea).  
Avoidance of large meals and low dietary intake of simple sugars improves these symptoms.



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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

after total gastrectomy, and accelerated emptying of hyperosmolar food boluses into the small bowel results in **dumping syndrome** (characterized by colicky abdominal pain, nausea, and diarrhea).

Avoidance of large meals and low dietary intake of simple sugars improves these symptoms.

**(Choices B, C, and D)** Pepsin and HCl are helpful, but not required, for protein digestion; patients can still digest protein after undergoing total gastrectomy due to the presence of pancreatic and intestinal proteases. It is not necessary to administer gastric enzymes, HCl, or hydrolyzed protein in these patients.

**(Choice E)** Medium-chain triglycerides can passively diffuse from the gastrointestinal lumen into enterocytes, but they are best absorbed after being degraded into monoglycerides and free fatty acids by lingual and pancreatic lipase. Supplementation is not necessary in total gastrectomy patients.

### Educational objective:

Intrinsic factor (IF) is a glycoprotein that is normally secreted by parietal cells in the stomach and is necessary for the absorption of vitamin B<sub>12</sub> in the ileum. Patients who have undergone a total gastrectomy require lifelong vitamin B<sub>12</sub> supplementation due to inability to produce IF.

### References

- Oral vitamin B12 replacement: an effective treatment for vitamin B12 deficiency after total gastrectomy in gastric cancer patients.



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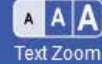
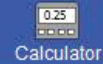
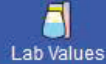
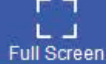
Feedback



Suspend



End Block



A 30-year-old man comes to the office due to a 4-month history of fatigue that is worse at the end of the day. The patient has also had abdominal bloating and intermittent loose stools after meals. His appetite is normal, and he has had no weight loss. Vital signs are normal. Examination shows pale mucosa. The abdomen is mildly distended and tympanic; there is no tenderness or organomegaly. Rectal examination reveals brown stool that is negative for fecal occult blood. Laboratory results are as follows:

Hematocrit	28%
Mean corpuscular volume	75 $\mu\text{m}^3$
Leukocytes	7,100/mm <sup>3</sup>
Platelets	490,000/mm <sup>3</sup>

C-reactive protein level is normal. Which of the following pathologic gastrointestinal tract findings is most likely to be present in this patient?

- ☐ A. Atrophic mucosa with loss of villi of the small intestine
- ☐ B. Autoimmune destruction of gastric parietal cells





Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Hematocrit

28%

Mean corpuscular volume 75  $\mu\text{m}^3$ Leukocytes 7,100/ $\text{mm}^3$ Platelets 490,000/ $\text{mm}^3$ 

C-reactive protein level is normal. Which of the following pathologic gastrointestinal tract findings is most likely to be present in this patient?

- ☐ A. Atrophic mucosa with loss of villi of the small intestine
- ☐ B. Autoimmune destruction of gastric parietal cells
- ☐ C. Chronic inflammation within the colonic mucosa and submucosa
- ☒ D. *Giardia* trophozoites lining the small intestinal mucosa
- ☐ E. Subepithelial collagen deposition in the colon

**Submit**





Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Hematocrit

26%

Mean corpuscular volume 75  $\mu\text{m}^3$ Leukocytes 7,100/ $\text{mm}^3$ Platelets 490,000/ $\text{mm}^3$ 

C-reactive protein level is normal. Which of the following pathologic gastrointestinal tract findings is most likely to be present in this patient?

- ☒ A. Atrophic mucosa with loss of villi of the small intestine (57%)
- ☐ B. Autoimmune destruction of gastric parietal cells (12%)
- ☐ C. Chronic inflammation within the colonic mucosa and submucosa (17%)
- ☐ D. *Giardia* trophozoites lining the small intestinal mucosa (7%)
- ☐ E. Subepithelial collagen deposition in the colon (4%)

Correct

57%



03 mins, 06 secs



11/13/2020

Block Time Remaining: 00:32:53

TUTOR

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Feedback



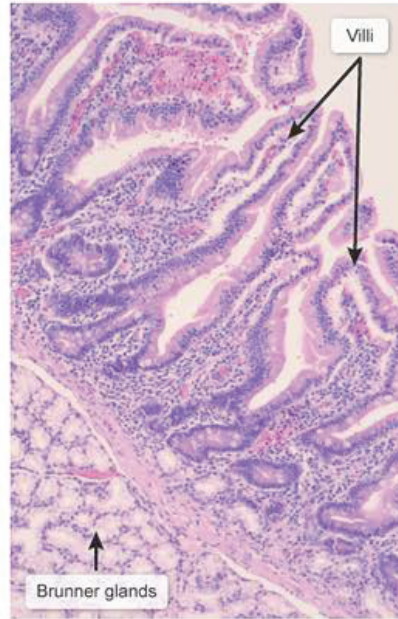
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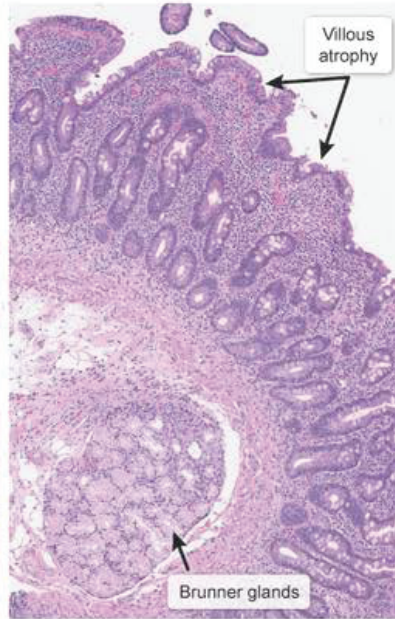
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Exhibit Display

Normal duodenum



Celiac disease



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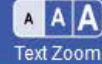
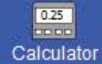
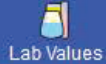
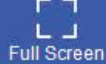
Zoom In

Zoom Out

Reset

New | Existing

My Notebook



This patient's loose stools, abdominal cramps, and microcytic anemia are most likely due to **celiac disease**, an immune-mediated disorder of the small bowel caused by dietary gluten. Gliadin, a component of gluten, is responsible for triggering the T-cell-mediated reaction against the small-bowel mucosa seen in celiac disease. This is initially characterized by intraepithelial lymphocytosis, followed as the disease progresses by a **loss of small-bowel intestinal villi** and **mucosal atrophy**. This decreases the nutritional absorptive capabilities of the small bowel, particularly in the duodenum and proximal jejunum.

Because iron is absorbed primarily in the duodenum, **iron deficiency** leading to **microcytic anemia** is a common manifestation of celiac disease; common presenting features include fatigue and pale mucosa. Other symptoms of gluten-sensitive enteropathy include **postprandial diarrhea** and steatorrhea (eg, pale, loose stools), **abdominal cramps**, bloating, flatulence, and weight loss. Celiac disease is not associated with elevated systemic inflammatory markers (eg, C-reactive protein, erythrocyte sedimentation rate), and unlike gastrointestinal disorders that cause chronic blood loss (eg, inflammatory bowel disease, colon cancer), in celiac disease, fecal occult blood testing is negative.

**(Choice B)** Pernicious anemia is characterized by antibody-mediated destruction of intrinsic factor and gastric parietal cells. This can lead to decreased **vitamin B<sub>12</sub> absorption**, with macrocytic (not microcytic) anemia, glossitis, and, sometimes, subacute combined degeneration of the dorsolateral spinal cord.







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

anemia, glossitis, and, sometimes, subacute combined degeneration of the dorsolateral spinal cord.

**(Choice C)** *Ulcerative colitis* causes chronic inflammatory changes of the colonic mucosa and submucosa. Iron deficiency anemia is common but is due to blood loss rather than malabsorption; a positive fecal occult blood test would be expected, and inflammatory markers are typically elevated.

**(Choice D)** Giardiasis is usually diagnosed on stool testing, although *Giardia lamblia* trophozoites are readily visible on small-bowel biopsy. Giardiasis is a common cause of diarrhea and may cause steatorrhea due to impairment of brush border enzymes. However, iron malabsorption with microcytic anemia is uncommon.

**(Choice E)** *Collagenous colitis* is characterized by subepithelial collagen deposition in the colon. It often causes watery diarrhea but does not affect iron absorption in the small intestine, so microcytic anemia would be unexpected.

### Educational objective:

Celiac disease is an immune-mediated disorder triggered by dietary gluten that causes small-bowel malabsorption. Because the proximal small bowel is primarily affected, iron deficiency leading to microcytic anemia is common. Histopathology is characterized by intraepithelial lymphocytosis, loss of intestinal villi, and mucosal atrophy.



1



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 78-year-old male nursing home resident is brought to the physician because of abdominal pain and discomfort. He has a history of advanced dementia and is only partially able to verbalize his symptoms. He has had intermittent abdominal discomfort for years, with no other related symptoms. He denies diarrhea and rectal bleeding but has not had a bowel movement in approximately 5 days. The patient is largely bed-bound, and only has minimal activity with the help of nurses and physical therapists. Past regular colonoscopies have shown only benign lesions. His other medical problems include dementia, coronary artery disease, hypertension, spinal stenosis, and osteoarthritis of his hips and knees. Abdominal examination does not show tenderness, masses, or hepatosplenomegaly, although fullness is appreciated. The remainder of the examination shows no abnormalities. Polyethylene glycol is administered and produces a bowel movement within 24 hours. The mechanism of action of polyethylene glycol in this patient is most similar to the pathophysiology of which of the following disorders?

- ☐ A. Irritable bowel syndrome
- ☒ B. Crohn's disease
- ☐ C. Lactase deficiency
- ☐ D. Carcinoid syndrome



Feedback



Suspend



End Block





diarrhea and rectal bleeding but has not had a bowel movement in approximately 5 days. The patient is largely bed-bound, and only has minimal activity with the help of nurses and physical therapists. Past regular colonoscopies have shown only benign lesions. His other medical problems include dementia, coronary artery disease, hypertension, spinal stenosis, and osteoarthritis of his hips and knees. Abdominal examination does not show tenderness, masses, or hepatosplenomegaly, although fullness is appreciated. The remainder of the examination shows no abnormalities. Polyethylene glycol is administered and produces a bowel movement within 24 hours. The mechanism of action of polyethylene glycol in this patient is most similar to the pathophysiology of which of the following disorders?

- ☐ A. Irritable bowel syndrome
- ☐ B. Crohn's disease
- ☐ C. Lactase deficiency
- ☐ D. Carcinoid syndrome
- ☐ E. Rectal prolapse

**Submit**

Block Time Remaining: 00:32:58

TUTOR

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Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

largely bed-bound, and only has minimal activity with the help of nurses and physical therapists. Past regular colonoscopies have shown only benign lesions. His other medical problems include dementia, coronary artery disease, hypertension, spinal stenosis, and osteoarthritis of his hips and knees. Abdominal examination does not show tenderness, masses, or hepatosplenomegaly, although fullness is appreciated. The remainder of the examination shows no abnormalities. Polyethylene glycol is administered and produces a bowel movement within 24 hours. The mechanism of action of polyethylene glycol in this patient is most similar to the pathophysiology of which of the following disorders?

- ☐ A. Irritable bowel syndrome (11%)
- ☐ B. Crohn's disease (2%)
- ☒ C. Lactase deficiency (76%)
- ☐ D. Carcinoid syndrome (8%)
- ☐ E. Rectal prolapse (1%)

Correct

76%

Answered correctly



01 min, 02 secs

Time spent



11/04/2020

Last updated

Block Time Remaining: 00:33:55

TUTOR

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0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Constipation is common in elderly, debilitated patients as well as those on chronic opiate therapy. Because lifestyle changes are not an option in patients such as this one, constipation in this population is commonly treated with osmotic laxatives (e.g., magnesium citrate, polyethylene glycol), stool softeners, and enemas.

Osmotic laxatives are nonabsorbable or poorly absorbable substances that attract water into the intestinal lumen, thus distending the intestinal wall and increasing peristalsis. The laxative effect is usually fairly rapid. Magnesium hydroxide (and other magnesium-containing compounds, such as magnesium citrate) is another osmotic laxative that is often used, although its efficacy is questionable and there is not enough evidence to support its widespread use.

Lactase deficiency is a disease state characterized by osmotic diarrhea. Inherited or acquired deficiency of the intestinal brush border enzyme lactase (i.e., disaccharidase) causes inability to break down lactose into glucose and galactose. Undigested lactose is a nonabsorbable osmotic substance, and its accumulation in the small intestine leads to an increase in the secretion of water and electrolytes into the intestinal lumen. Lactase deficiency (i.e., lactose intolerance) presents with abdominal pain and distension and watery diarrhea. Abdominal pain and distention result from the metabolism of lactose by normal gut flora through fermentation, which causes the production of gas. The symptoms resolve when milk-containing products are eliminated from the diet.



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

are eliminated from the diet.

**(Choice A)** Irritable bowel syndrome is a functional intestinal disorder that presents with diarrhea alternating with constipation, abdominal pain, and distention without organic cause. Fecal water and electrolyte content are normal.

**(Choice B)** Diarrhea in Crohn's disease is of the secretory type, which is characterized by high electrolyte content due to poor absorption and increased losses from the inflamed intestinal mucosa.

**(Choice D)** Diarrhea in carcinoid syndrome is secretory and high in electrolytes.

**(Choice E)** Rectal prolapse is a protrusion of rectal mucosa through the anus associated with pregnancy and constipation; it can also be seen in severe diarrhea. Another important cause of rectal prolapse is cystic fibrosis, particularly in children.

### Educational objective:

Polyethylene glycol is an osmotic laxative. Diarrhea associated with lactase deficiency is also osmotic and occurs due to accumulation of nonabsorbable lactose in the intestinal lumen. Magnesium hydroxide (and other magnesium-containing compounds, such as magnesium citrate) is another osmotic laxative that is often used, although its efficacy is questionable and there is not enough evidence to support its widespread use.



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Feedback



Suspend



End Block





A 43-year-old woman comes to the office with a 1-month history of dull abdominal pain that occurs mainly after eating. The pain is localized to the right upper quadrant and is especially severe after fatty meals. Physical examination is unremarkable. Ultrasound of the abdomen reveals several mobile echogenic foci within the gallbladder lumen. Which of the following sets of conditions is most likely present within this patient's gallbladder?

Cholesterol	Bile acids	Phosphatidylcholine
<input type="radio"/> A. ↓	↑	↑
<input type="radio"/> B. ↓	↑	↓
<input type="radio"/> C. ↓	↓	↑
<input type="radio"/> D. ↑	↓	↓
<input type="radio"/> E. ↑	↑	↓
<input type="radio"/> F. ↑	↓	↑



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

after eating. The pain is localized to the right upper quadrant and is especially severe after fatty meals. Physical examination is unremarkable. Ultrasound of the abdomen reveals several mobile echogenic foci within the gallbladder lumen. Which of the following sets of conditions is most likely present within this patient's gallbladder?

	Cholesterol	Bile acids	Phosphatidylcholine	
<input type="radio"/> A. ↓		↑	↑	(2%)
<input type="radio"/> B. ↓		↑	↓	(2%)
<input type="radio"/> C. ↓		↓	↑	(1%)
<input checked="" type="radio"/> D. ↑		↓	↓	(51%)
<input type="radio"/> E. ↑		↑	↓	(20%)
<input type="radio"/> F. ↑		↓	↑	(22%)

Correct

51%



36 secs



12/28/2020

Block Time Remaining: 00:34:31

TUTOR

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1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

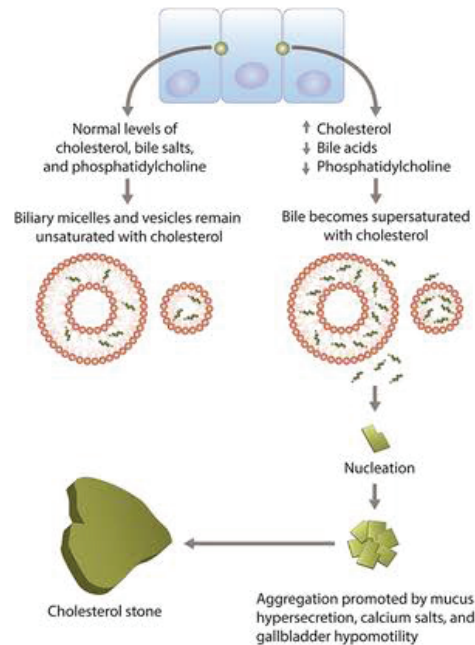
Reverse Color

Text Zoom

Settings

## Exhibit Display

## Pathogenesis of cholesterol gallstones



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Zoom Out

Reset

New | Existing

My Notebook



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Removal of excess cholesterol from the body occurs via 2 mechanisms: excretion of **free cholesterol** into bile and conversion of cholesterol into **bile acids**.

In the liver, free cholesterol is converted into cholic and chenodeoxycholic acids through a series of chemical reactions beginning with cholesterol 7 $\alpha$ -hydroxylase (rate-limiting step in bile acid synthesis). These bile acids are then conjugated to either glycine or taurine (improving solubility and emulsifying ability) to create the bile salts that are actively secreted into the bile canaliculi. As **water-insoluble cholesterol** is secreted in bile, it is rendered soluble in small amounts by the detergent action of these amphipathic (eg, hydrophobic and hydrophilic) bile salts and phosphatidylcholine (a phospholipid). When there is more cholesterol than can be made soluble, it **precipitates into crystals** that eventually grow and merge to form **gallstones**. Gallbladder hypomotility further promotes cholesterol nucleation and gallstone formation.

**(Choices A, B, C, E, and F)** These represent lower cholesterol concentrations related to total bile salt and phosphatidylcholine levels. Such conditions would decrease the likelihood of gallstone formation.

### Educational objective:

Elevated cholesterol concentrations increase the likelihood of cholesterol precipitation and gallstone formation. High levels of bile salts and phosphatidylcholine increase cholesterol solubility and decrease the



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

These bile acids are then conjugated to either glycine or taurine (improving solubility and emulsifying ability) to create the bile salts that are actively secreted into the bile canaliculi. As **water-insoluble cholesterol** is secreted in bile, it is rendered soluble in small amounts by the detergent action of these amphipathic (eg, hydrophobic and hydrophilic) bile salts and phosphatidylcholine (a phospholipid). When there is more cholesterol than can be made soluble, it **precipitates into crystals** that eventually grow and merge to form **gallstones**. Gallbladder hypomotility further promotes cholesterol nucleation and gallstone formation.

**(Choices A, B, C, E, and F)** These represent lower cholesterol concentrations related to total bile salt and phosphatidylcholine levels. Such conditions would decrease the likelihood of gallstone formation.

### Educational objective:

Elevated cholesterol concentrations increase the likelihood of cholesterol precipitation and gallstone formation. High levels of bile salts and phosphatidylcholine increase cholesterol solubility and decrease the risk of gallstones.

### References

- Pathogenesis of gallstones
- Pathogenesis of gallstones



1



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

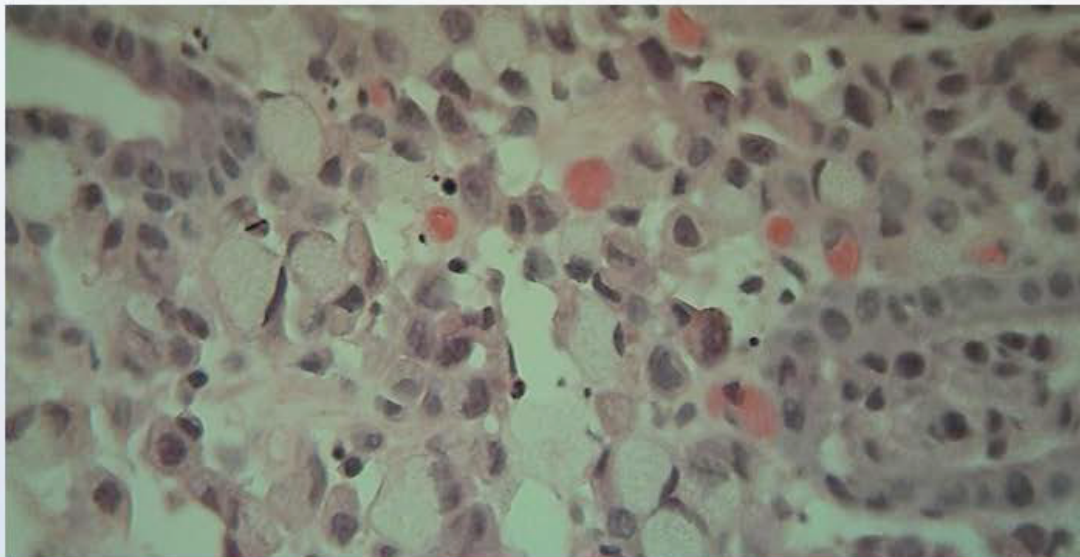


Text Zoom



Settings

A 59-year-old man is evaluated in the clinic for recent unintentional weight loss. He says, "My pants are fitting a lot looser than usual." The patient also has epigastric discomfort after meals with occasional nausea. He reports that food is not as appetizing as it used to be. He has no known medical problems and takes no medications. The patient's father has a history of peptic ulcer disease. Upper endoscopy shows a lesion in the stomach that is biopsied and displayed in the slide below.



0



Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



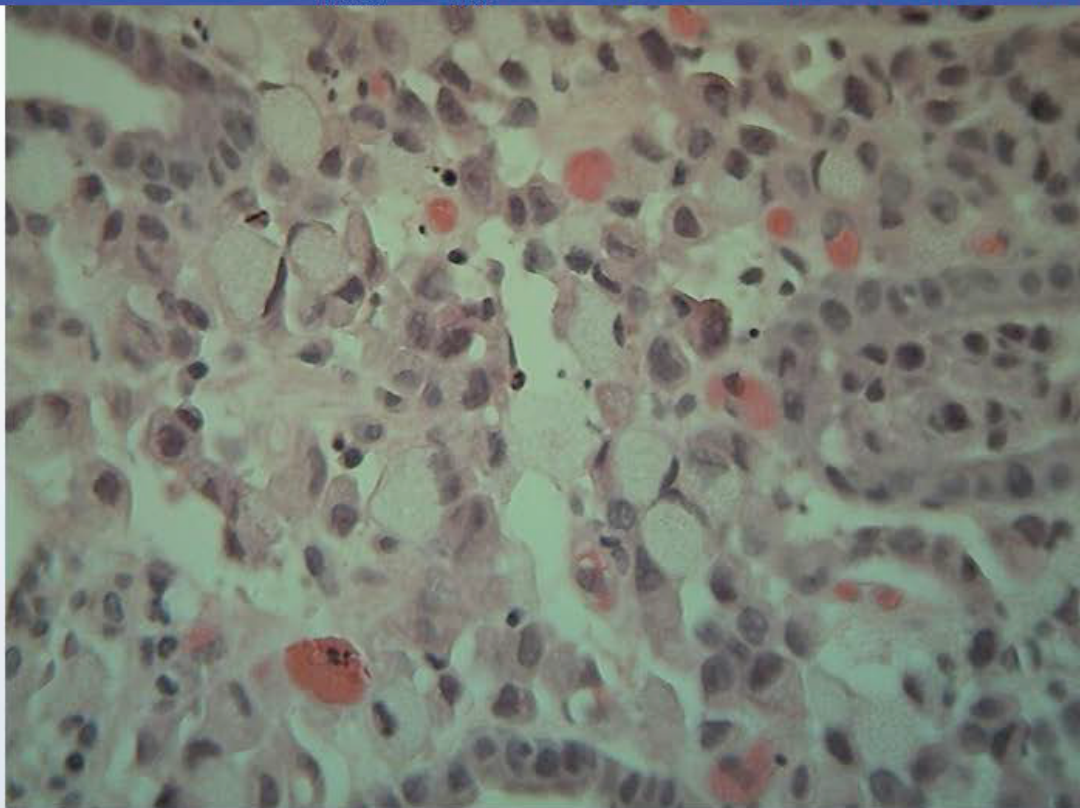
Reverse Color



Text Zoom



Settings



The lesion most likely demonstrates which of the following?

Block Time Remaining: 00:34:37

TUTOR

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



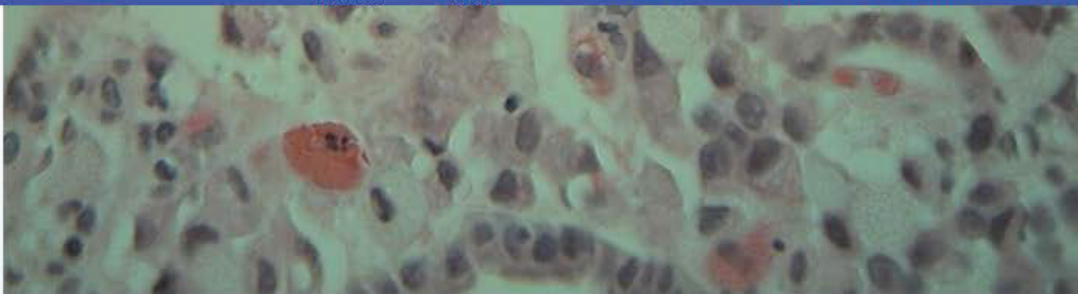
Reverse Color



Text Zoom



Settings



The lesion most likely demonstrates which of the following?

- ☐ A. Deep ulceration and vessel erosion
- ☐ B. Infiltrative growth within the stomach wall
- ☐ C. Progressive mucosal atrophy
- ☐ D. Rapid intraluminal expansion
- ☐ E. Rugal thickening with acid hypersecretion

**Submit**

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



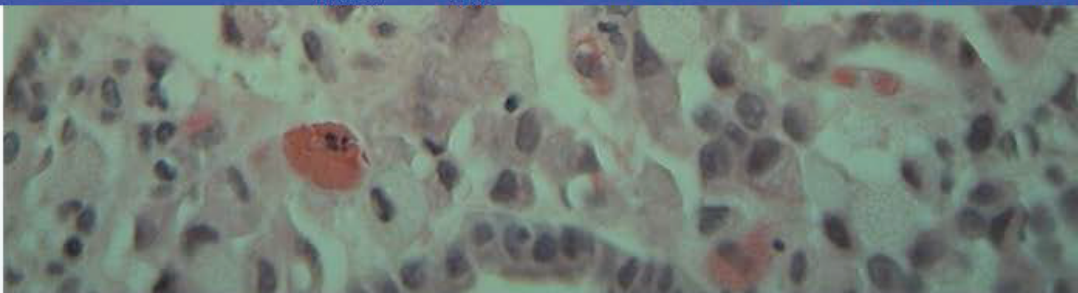
Reverse Color



Text Zoom



Settings



The lesion most likely demonstrates which of the following?

- ☐ A. Deep ulceration and vessel erosion (13%)
- ☒ B. Infiltrative growth within the stomach wall (52%)
- ☐ C. Progressive mucosal atrophy (12%)
- ☐ D. Rapid intraluminal expansion (3%)
- ☐ E. Rugal thickening with acid hypersecretion (17%)

Correct

52%



22 secs



01/09/2021

Block Time Remaining: 00:34:53

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



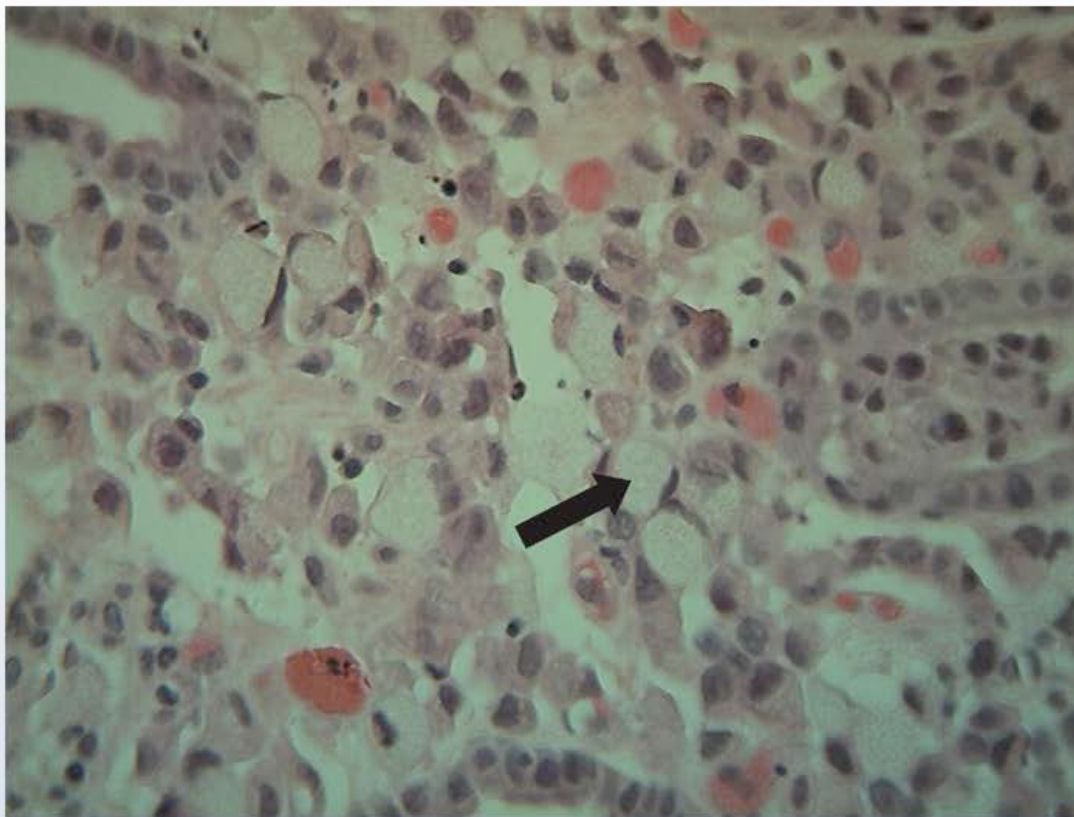
Reverse Color



Text Zoom



Settings



Block Time Remaining: 00:34:53

TUTOR

<https://t.me/USMLEWorldStep1>

0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This slide shows typical features of **signet-ring carcinoma**, 1 of 2 major types of **gastric adenocarcinoma**. Signet-ring carcinomas consist of cells that do not form glands. Cells often contain abundant mucin droplets that push the nucleus to one side and lead to the characteristic appearance of a **signet ring**. On gross examination, signet-ring carcinomas are characterized by **diffuse** involvement of the stomach wall (due to loss of the cell adhesion protein **E-cadherin**). They have a plaquelike appearance, are ill-defined, and often infiltrate large areas of the stomach wall, causing a "leather-bottle stomach" (**linitis plastica**).

**Intestinal-type adenocarcinomas** of the stomach closely resemble colon cancers, showing well-formed glands that consist of columnar or cuboidal cells. They tend to grow as nodular, polypoid, and well-demarcated masses that rapidly expand within the gastric lumen (**Choice D**). These lesions often ulcerate/bleed and must be differentiated from peptic gastric ulcers by biopsy (**Choice A**).

The most important factors that influence survival rate with gastric adenocarcinoma are the depth of invasion through the gastric wall and regional lymph node involvement. Metastasis is often present at the time of diagnosis and most commonly involves the **supraclavicular** lymph node (Virchow node) and **periumbilical** nodes (Sister Mary Joseph nodule).

(Choice C) Chronic gastritis is most commonly associated with *Helicobacter pylori* infection. Long



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

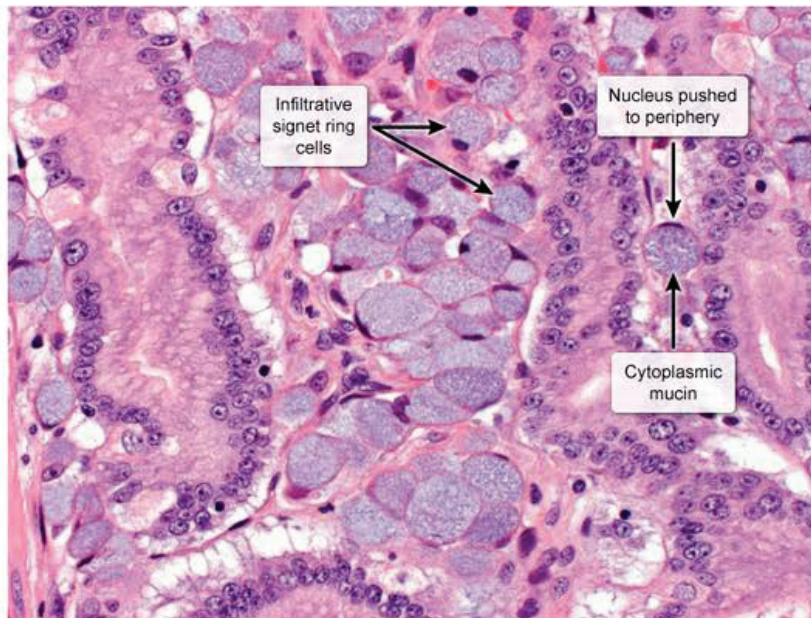
Reverse Color

Text Zoom

Settings

## Exhibit Display

## Diffuse-type gastric adenocarcinoma



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New | Existing

My Notebook

Block Time Remaining: 00:34:53

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice C)** Chronic gastritis is most commonly associated with *Helicobacter pylori* infection. Long-standing inflammation of the gastric mucosa can lead to diffuse gland atrophy and intestinal metaplasia. Chronic gastric inflammation increases the risk of gastric carcinomas.

**(Choice E)** Rugal thickening with acid hypersecretion is a characteristic finding in the stomach of a patient with Zollinger-Ellison syndrome. Rugal hypertrophy with parietal cell atrophy and decreased acid secretion occurs with Ménétrier disease.

### Educational objective:

There are 2 morphological variants of gastric adenocarcinoma. The intestinal type forms a solid mass that projects into the stomach lumen and is composed of glandular-forming cuboidal or columnar cells. In contrast, diffuse carcinoma (linitis plastica) infiltrates the stomach wall and displays signet-ring cells on light microscopy.

### References

- Gastric cancer: Classification, histology and application of molecular pathology.
- Pathology and molecular biology of gastric cancer.

Pathology

Gastrointestinal &amp; Nutrition

Gastric cancer

Block Time Remaining: 00:34:53

TUTOR

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



A 58-year-old man is being evaluated for constipation and weight loss over the last several months. During the past 2 weeks, he has had several episodes of rectal bleeding. The patient has never had a screening colonoscopy. Examination shows a soft and nontender abdomen without masses or organomegaly. Digital rectal examination reveals a firm palpable mass in the rectal vault. Flexible rectosigmoidoscopy shows a large ulcerative mass in the middle third of the rectum extending to the rectosigmoid junction. He undergoes surgical resection of the rectosigmoid colon. Frozen section analysis reveals clear margins of the colon specimen with metastases in the pararectal lymph nodes. Which of the following lymph node groups should be sampled in this patient for further assessment of metastatic disease?

- ☐ A. Celiac
- ☐ B. Internal iliac
- ☐ C. Left colic
- ☐ D. Right colic
- ☐ E. Superficial inguinal
- ☐ F. Superior mesenteric





the past 2 weeks, he has had several episodes of rectal bleeding. The patient has never had a screening colonoscopy. Examination shows a soft and nontender abdomen without masses or organomegaly. Digital rectal examination reveals a firm palpable mass in the rectal vault. Flexible rectosigmoidoscopy shows a large ulcerative mass in the middle third of the rectum extending to the rectosigmoid junction. He undergoes surgical resection of the rectosigmoid colon. Frozen section analysis reveals clear margins of the colon specimen with metastases in the pararectal lymph nodes. Which of the following lymph node groups should be sampled in this patient for further assessment of metastatic disease?

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- ☐ B. Internal iliac
- ☐ C. Left colic
- ☐ D. Right colic
- ☐ E. Superficial inguinal
- ☐ F. Superior mesenteric
- ☐ G. Supraclavicular







rectal examination reveals a firm palpable mass in the rectal vault. Flexible rectosigmoidoscopy shows a large ulcerative mass in the middle third of the rectum extending to the rectosigmoid junction. He undergoes surgical resection of the rectosigmoid colon. Frozen section analysis reveals clear margins of the colon specimen with metastases in the pararectal lymph nodes. Which of the following lymph node groups should be sampled in this patient for further assessment of metastatic disease?

- ☐ A. Celiac (1%)
- ☒ B. Internal iliac (53%)
- ☐ C. Left colic (18%)
- ☐ D. Right colic (1%)
- ☐ E. Superficial inguinal (13%)
- ☐ F. Superior mesenteric (7%)
- ☐ G. Supraclavicular (4%)

Correct

53%



01 min, 32 secs



12/04/2020

Block Time Remaining: 00:36:25

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Feedback



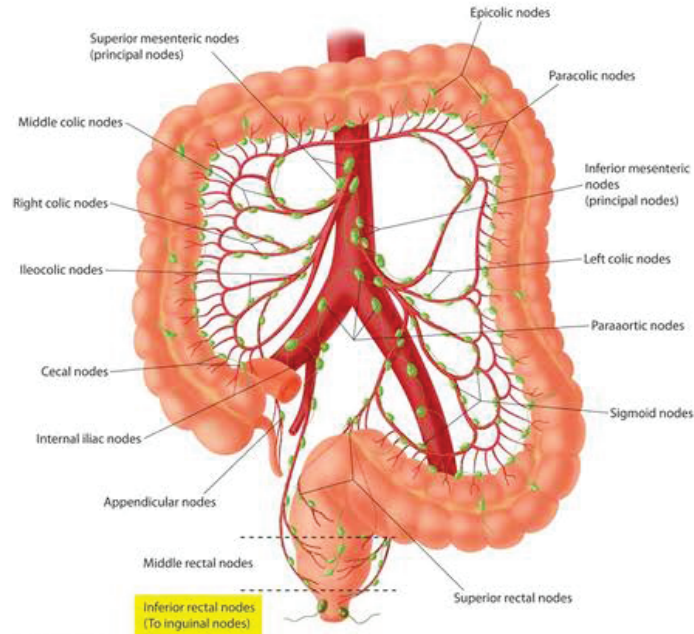
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End Block

### Exhibit Display

#### Lymph nodes & vessels of large intestine



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

**Lymphatic drainage** of the colon generally follows the arterial supply. Lymph nodes are located on the bowel wall (epicolic nodes), inner bowel margins along the arterial arcades (paracolic nodes), around the corresponding mesenteric vessels (intermediate nodes), and at the origin of the superior and inferior mesenteric arteries (principal nodes). The sentinel lymph nodes (first 1-4 lymph nodes draining a specific colonic segment) are usually the first site for colon cancer metastasis.

Lymphatic channels **proximal** to the anal **dentate line** drain into the **inferior mesenteric** and **internal iliac lymph nodes**. The upper rectum and superior part of the middle rectum follow the superior rectal nodes along the superior rectal artery into the inferior mesenteric lymph nodes. The middle to lower third of the rectum can drain upward into the inferior mesenteric nodes or follow the middle rectal nodes along the middle rectal artery to the internal iliac lymph nodes. Areas **distal** to the anal dentate line drain primarily into the **inguinal nodes**, although some lymph can also reach the inferior mesenteric and internal iliac nodes.

**(Choice A)** The celiac lymph nodes are located around the celiac trunk and drain lymph from the gastric, hepatic, and splenic nodes. These in turn drain their respective organ systems (not the colon).

**(Choice C)** The left colic lymph nodes and their branches are located along the left colic artery and drain the left colonic flexure and upper descending colon.



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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hepatic, and splenic nodes. These in turn drain their respective organ systems (not the colon).

**(Choice C)** The left colic lymph nodes and their branches are located along the left colic artery and drain the left colonic flexure and upper descending colon.

**(Choice D)** The right colic lymph nodes are found along the right colic artery and primarily drain the upper ascending colon.

**(Choice E)** The superficial inguinal lymph nodes lie below the inguinal ligament and are bordered by the sartorius and adductor longus muscles. They drain parts of the genitalia (eg, penis, scrotum, perineum, and vulva), buttocks, anus below the dentate line, and abdominal wall below the umbilicus.

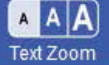
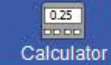
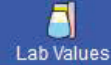
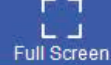
**(Choice F)** The superior mesenteric lymph nodes (mesenteric, ileocolic, and mesocolic) mainly drain the ileum, jejunum, vermiform process, and parts of the ascending and transverse colon.

**(Choice G)** Lymph node metastasis typically occurs sequentially through the epicolic/paracolic, intermediate, and paraaortic lymph nodes. Later in the disease course, the cancer can spread via the thoracic duct to the supraclavicular lymph node (Virchow node).

### Educational objective:

Lymphatic drainage of the rectum proximal to the anal dentate line occurs via the inferior mesenteric and internal iliac lymph nodes. Areas distal to the dentate line drain primarily into the inguinal nodes.





ascending colon.

**(Choice E)** The superficial inguinal lymph nodes lie below the inguinal ligament and are bordered by the sartorius and adductor longus muscles. They drain parts of the genitalia (eg, penis, scrotum, perineum, and vulva), buttocks, anus below the dentate line, and abdominal wall below the umbilicus.

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### Educational objective:

Lymphatic drainage of the rectum proximal to the anal dentate line occurs via the inferior mesenteric and internal iliac lymph nodes. Areas distal to the dentate line drain primarily into the inguinal nodes.

Anatomy  
Subject

Gastrointestinal & Nutrition  
System

Lymphatic drainage  
Topic

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Previous



Next



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Notes



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Settings

Rats exposed to high concentrations of carbon tetrachloride suffer rapid and extensive liver damage. Light microscopic examination of affected liver specimens shows fatty change and hepatocyte necrosis. These changes are the result of:

- ☐ A. Hypoperfusion
- ☐ B. Hypoxia
- ☐ C. Abnormal signal transduction
- ☐ D. Free radical injury
- ☐ E. Mitochondrial dysfunction

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Mark

Previous

Next

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Lab Values

Notes

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Settings

Rats exposed to high concentrations of carbon tetrachloride suffer rapid and extensive liver damage. Light microscopic examination of affected liver specimens shows fatty change and hepatocyte necrosis. These changes are the result of:

- ☐ A. Hypoperfusion (1%)
- ☐ B. Hypoxia (3%)
- ☐ C. Abnormal signal transduction (2%)
- ☒ D. Free radical injury (73%)
- ☐ E. Mitochondrial dysfunction (19%)

Correct



73%

Answered correctly



53 secs

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01/30/2021

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Explanation



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Previous



Next



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Tutorial



Lab Values



Notes



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Settings

Carbon tetrachloride ( $\text{CCl}_4$ ) causes free radical injury. Like many other toxic substances,  $\text{CCl}_4$  is oxidized by the P450 oxidase system in the liver. The result is the formation of the free radical  $\text{CCl}_3$ , which reacts with structural lipids of cell membranes. The result is lipid degradation and hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) formation. This process is called **lipid peroxidation**. The peroxides go on to form new radicals, continuing the vicious circle of lipid degradation. Carbon tetrachloride cell injury develops rapidly and leads to swelling of the endoplasmic reticulum, destruction of mitochondria, and increased permeability of cell membranes. These processes culminate in hepatocyte necrosis.

**(Choices A and B)** Hypoperfusion and hypoxia lead to tissue ischemia and necrosis. Carbon tetrachloride does not affect tissue oxygenation.

**(Choice C)** Abnormal signal transduction is a mechanism of oncogenesis, as occurs with mutations of the *Ras* proto-oncogene. This mutation increases cell sensitivity to mitogenic influences.

**(Choice E)** Mitochondrial dysfunction occurs in  $\text{CCl}_4$  intoxication as a result of free radical injury.

### Educational Objective:

The P450 microsomal oxidase system plays an important role in detoxification. In carbon tetrachloride poisoning, however, it produces free radicals that start a vicious cycle of hepatic injury.



Feedback



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Previous



Next



Full Screen



Tutorial



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Notes



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formation. This process is called **lipid peroxidation**. The peroxides go on to form new radicals, continuing the vicious circle of lipid degradation. Carbon tetrachloride cell injury develops rapidly and leads to swelling of the endoplasmic reticulum, destruction of mitochondria, and increased permeability of cell membranes. These processes culminate in hepatocyte necrosis.

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**(Choice E)** Mitochondrial dysfunction occurs in  $\text{CCl}_4$  intoxication as a result of free radical injury.

### Educational Objective:

The P450 microsomal oxidase system plays an important role in detoxification. In carbon tetrachloride poisoning, however, it produces free radicals that start a vicious cycle of hepatic injury.

Pathology

Gastrointestinal &amp; Nutrition

Acute liver failure

Subject

System

Topic

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Mark



Previous



Next



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Settings

A 32-year-old man comes to the clinic due to several months of fatigue and weight loss. The patient has no significant medical history. He drinks 1 or 2 alcoholic beverages daily and has used illicit intravenous drugs in the past. He is sexually active with his girlfriend. The patient has a maternal aunt with hypothyroidism, but his family history is otherwise unremarkable. Temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, pulse is 65/min, and respirations are 18/min. Physical examination is normal. A liver biopsy is obtained, and light microscopy reveals large hepatocytes filled with finely granular, homogeneous, pale pink cytoplasm. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Alcoholic steatohepatitis
- ☐ B. Hemochromatosis
- ☐ C. Hepatitis B infection
- ☐ D. Hepatitis C infection
- ☐ E. Nonalcoholic steatohepatitis

**Submit**

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Previous



Next



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Tutorial



Lab Values



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Text Zoom



Settings

A 32-year-old man comes to the clinic due to several months of fatigue and weight loss. The patient has no significant medical history. He drinks 1 or 2 alcoholic beverages daily and has used illicit intravenous drugs in the past. He is sexually active with his girlfriend. The patient has a maternal aunt with hypothyroidism, but his family history is otherwise unremarkable. Temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, pulse is 65/min, and respirations are 18/min. Physical examination is normal. A liver biopsy is obtained, and light microscopy reveals large hepatocytes filled with finely granular, homogeneous, pale pink cytoplasm. Which of the following is the most likely diagnosis in this patient?

- ☐ A. Alcoholic steatohepatitis (26%)
- ☐ B. Hemochromatosis (4%)
- ☒ C. Hepatitis B infection (34%)
- ☐ D. Hepatitis C infection (26%)
- ☐ E. Nonalcoholic steatohepatitis (8%)



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Mark



Previous



Next



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Tutorial



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Notes



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Settings

**Hepatitis B infection**, one of the most common causes of hepatic injury in the United States, is frequently transmitted sexually or via percutaneous inoculation (eg, intravenous drug use). A distinct histopathologic manifestation of **chronic** hepatitis B infection is the accumulation of hepatitis B **surface antigen** within infected hepatocytes. This results in the appearance of a finely granular, **diffusely homogeneous, pale eosinophilic** cytoplasm ("**ground-glass**" hepatocytes).

Other nonspecific morphologic changes include hepatocyte necrosis (eg, ballooning degeneration), apoptosis, steatosis, and portal inflammation with mononuclear inclusions (lymphocytes, macrophages). Acidophil (Councilman) bodies, deeply eosinophilic globules that represent shrunken apoptotic hepatocytes, can be seen in a variety of liver diseases.

**(Choices A and E)** **Hepatic steatosis** is characterized by the accumulation of large and small vesicles of fat within hepatocytes. It is most commonly due to significant alcohol ingestion (>15 drinks/week for men, >10 drinks/week for women) but can also be due to obesity (nonalcoholic steatohepatitis). **Mallory bodies** may be seen in alcoholic steatohepatitis; they are characterized by **clumped**, amorphous, eosinophilic intracytoplasmic inclusions made up of tangled intermediate filaments.

**(Choice B)** **Hemochromatosis** is characterized by the deposition of iron in the liver, which appears as gold-



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Settings

>10 drinks/week for women) but can also be due to obesity (nonalcoholic steatohepatitis). **Mallory bodies** may be seen in alcoholic steatohepatitis; they are characterized by **clumped**, amorphous, eosinophilic intracytoplasmic inclusions made up of tangled intermediate filaments.

**(Choice B)** **Hemochromatosis** is characterized by the deposition of iron in the liver, which appears as gold-yellow hemosiderin granules in the cytoplasm. Cirrhosis and portal hypertension result if the condition is left untreated.

**(Choice D)** A liver infected with hepatitis C virus commonly has lymphoid aggregates within the portal tracts and focal areas of macrovesicular steatosis; however, ground-glass hepatocytes are more specific for hepatitis B infection.

### Educational objective:

Hepatitis B infection causes the hepatocellular cytoplasm to fill with hepatitis B surface antigen. These inclusions are highly specific for hepatitis B infection and have a finely granular, pale eosinophilic, ground-glass appearance.

### References

- "Ground-glass" hepatocytes.

• Liver biopsy findings in chronic hepatitis B



0



Feedback



Suspend



End Block

A 1-month-old boy is brought to the office for follow-up of blood-streaked stools and diarrhea. The patient was born preterm at 35 weeks gestation and had no complications in the newborn nursery. He had been taking a standard cow's milk-based formula until 2 weeks ago when he developed loose stools streaked with blood and mucus. Symptoms resolved after changing the formula. If histopathologic examination had been performed when the patient was symptomatic, which of the following would most likely be seen?

- ☐ A. Eosinophilic infiltration in the distal colon
- ☐ B. Hemorrhagic necrosis of the bowel wall
- ☐ C. Heterotopic gastric mucosa in the distal ileum
- ☐ D. Neutrophilic crypt abscess formation in the colon

Submit



A 1-month-old boy is brought to the office for follow-up of blood-streaked stools and diarrhea. The patient was born preterm at 35 weeks gestation and had no complications in the newborn nursery. He had been taking a standard cow's milk-based formula until 2 weeks ago when he developed loose stools streaked with blood and mucus. Symptoms resolved after changing the formula. If histopathologic examination had been performed when the patient was symptomatic, which of the following would most likely be seen?

- ☒ A. Eosinophilic infiltration in the distal colon (43%)
- ☐ B. Hemorrhagic necrosis of the bowel wall (28%)
- ☐ C. Heterotopic gastric mucosa in the distal ileum (12%)
- ☐ D. Neutrophilic crypt abscess formation in the colon (15%)

**Incorrect**

Correct answer

A



43%

Answered correctly



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Time Spent



03/06/2021

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Explanation

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End Block



Food protein–induced allergic proctocolitis	
Pathophysiology	<ul style="list-style-type: none"> <li>• Non-IgE-mediated reaction</li> <li>• Eosinophilic inflammation of rectosigmoid colon</li> <li>• Common triggers: cow's milk &amp; soy protein</li> </ul>
Clinical features	<ul style="list-style-type: none"> <li>• Age 1-4 weeks (up to 6 months)</li> <li>• Well appearing</li> <li>• Blood- &amp;/or mucus-streaked stools (positive Hemoccult)</li> </ul>
Treatment & prognosis	<ul style="list-style-type: none"> <li>• Protein elimination (eg, hydrolyzed formula)</li> <li>• Tolerance of offending protein by age 1</li> </ul>

This patient most likely has **food protein–induced allergic proctocolitis**, a benign condition of early infancy (age <6 months). Affected infants have a **non-IgE-mediated reaction** to proteins found in breast milk or formula (most common trigger is cow's milk). **Painless, blood-streaked stools** (which may also be loose and contain mucus) typically develop weeks to months after initial exposure to the food allergen.

Diagnosis is clinical. Although endoscopy is not performed unless symptoms are atypical (eg, severe bleeding, constipation, vomiting), characteristic findings include **inflammation** (ie, erythema, edema)



breeding, constipation, vomiting), characteristic findings include **inflammation** (ie, erythema, edema)

confined to the **distal colon** and rectum. Histopathology findings include infiltration of **eosinophils** within the lamina propria and muscularis mucosa.

Management includes dietary avoidance of the trigger protein (eg, switching to a hydrolyzed formula, maternal elimination of dairy for breastfed infants). Symptoms typically resolve within weeks, and most infants can tolerate the offending protein by age 1.

**(Choice B)** Hemorrhagic necrosis of the bowel wall describes **necrotizing enterocolitis**, a gastrointestinal emergency that can result in gut ischemia and death if untreated (eg, bowel rest, antibiotics). In addition to rectal bleeding, patients often have abdominal distension, poor feeding, and hemodynamic instability, none of which is present in this patient.

**(Choices C and D)** A Meckel diverticulum can contain **heterotopic gastric mucosa** in the distal ileum, and **neutrophilic crypt abscesses** can be seen with ulcerative colitis. Although these conditions, which are both exceedingly rare in the neonatal period, can cause blood in the stool, neither would resolve with a change in formula.

### Educational objective:

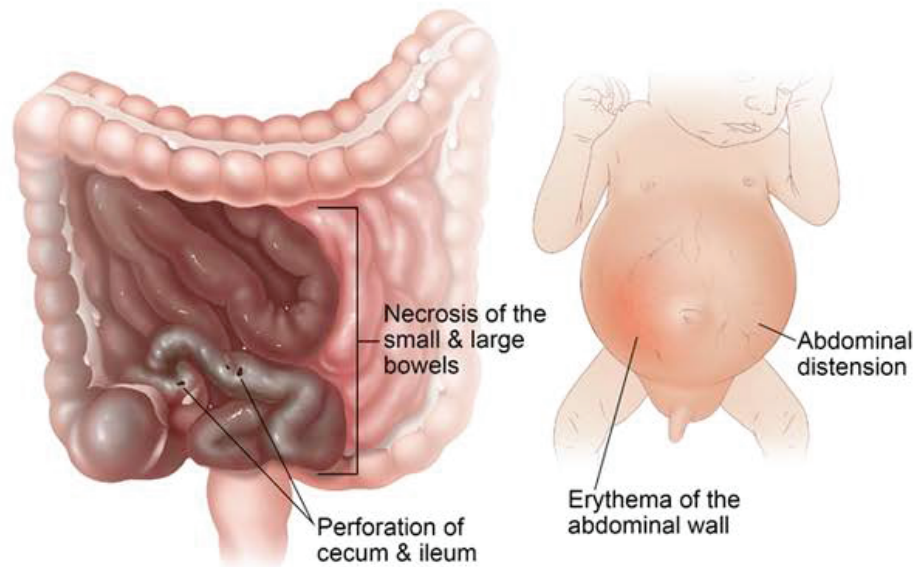
Food protein–induced allergic proctocolitis is a non–IgE-mediated reaction that causes inflammation and eosinophilic infiltration of the distal colon. Classic presentation is in early infancy with painless, blood-



bleeding, constipation, vomiting), characteristic findings include inflammation (ie, erythema, edema)

## Exhibit Display

## Necrotizing enterocolitis



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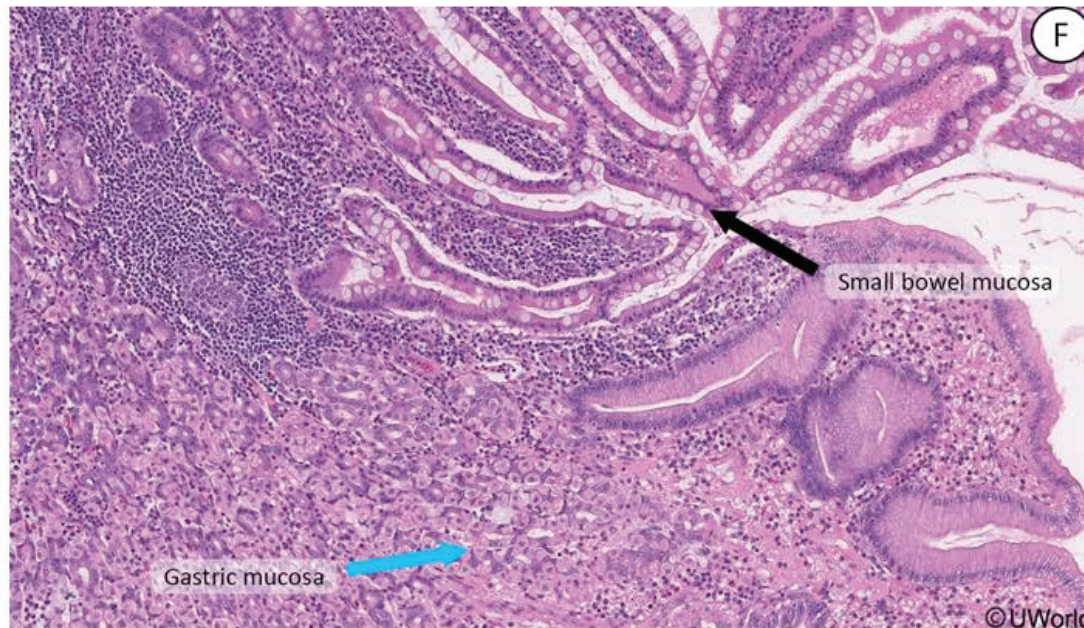
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bleeding, constipation, vomiting), characteristic findings include inflammation (ie, erythema, edema)

Exhibit Display



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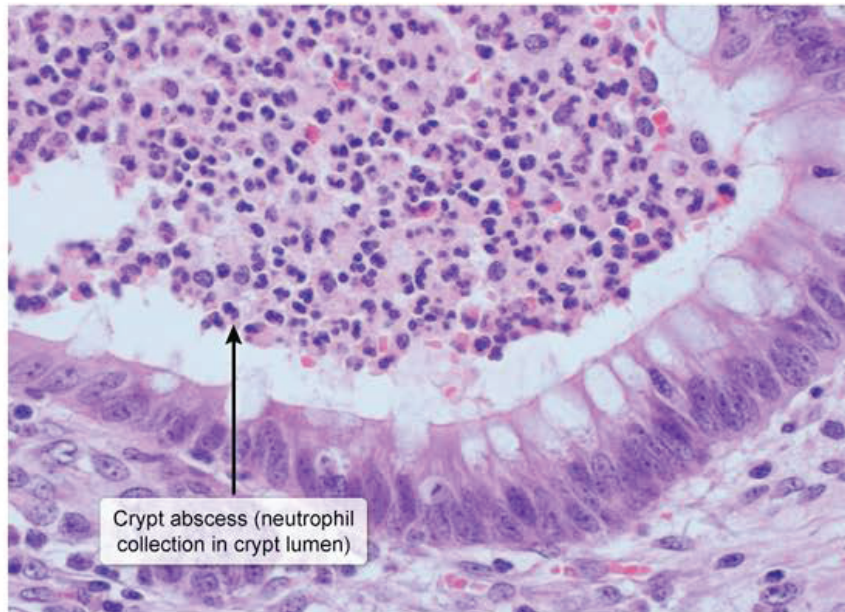
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bleeding, constipation, vomiting), characteristic findings include inflammation (ie, erythema, edema)

## Exhibit Display

## Ulcerative colitis



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**(Choice B)** Hemorrhagic necrosis of the bowel wall describes [necrotizing enterocolitis](#), a gastrointestinal emergency that can result in gut ischemia and death if untreated (eg, bowel rest, antibiotics). In addition to rectal bleeding, patients often have abdominal distension, poor feeding, and hemodynamic instability, none of which is present in this patient.

**(Choices C and D)** A Meckel diverticulum can contain [heterotopic gastric mucosa](#) in the distal ileum, and [neutrophilic crypt abscesses](#) can be seen with ulcerative colitis. Although these conditions, which are both exceedingly rare in the neonatal period, can cause blood in the stool, neither would resolve with a change in formula.

### Educational objective:

Food protein–induced allergic proctocolitis is a non–IgE-mediated reaction that causes inflammation and eosinophilic infiltration of the distal colon. Classic presentation is in early infancy with painless, blood-streaked stools that resolve with dietary avoidance of the offending food protein (eg, cow's milk).

### References

- [Food protein–induced enterocolitis syndrome and allergic proctocolitis.](#)

Pathology

Gastrointestinal &amp; Nutrition

Food protein-induced allergic proctocolitis

Subject

System

Topic







A 17-year-old girl is brought to the office due to yellow eyes for the past day. The patient has no other symptoms, including fever, rash, abdominal pain, vomiting, or diarrhea. She has been preparing for her high school exit examination and has been quite stressed. Temperature is 37.1 C (98.8 F), blood pressure is 110/78 mm Hg, pulse is 80/min, and respirations are 14/min. Mild scleral icterus is present. The abdomen is soft with no hepatosplenomegaly. Serum laboratory results are as follows:

Hemoglobin	13.1 g/dL
Bilirubin, total	3.3 mg/dL
Bilirubin, direct	0.5 mg/dL
Aspartate aminotransferase (SGOT)	22 U/L
Alanine aminotransferase (SGPT)	21 U/L

Two weeks after her examination, the patient's symptoms resolve. Repeat testing shows a total bilirubin concentration of 1.5 mg/dL. Which of the following changes most likely contributed to this patient's hyperbilirubinemia?

Hematoctrit

Hematoctrit

Bilirubin



1  
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Two weeks after her examination, the patient's symptoms resolve. Repeat testing shows a total bilirubin concentration of 1.5 mg/dL. Which of the following changes most likely contributed to this patient's hyperbilirubinemia?

**Hepatocyte  
bilirubin storage**

**Hepatocyte  
bilirubin  
excretion**

**Bilirubin  
conjugation**

- ☐ A. Decreased      Decreased      Decreased
- ☐ B. Decreased      Increased      Increased
- ☐ C. Increased      Decreased      Normal
- ☐ D. Increased      Increased      Normal
- ☐ E. Increased      Normal      Decreased
- ☐ F. Normal      Normal      Decreased





Two weeks after her examination, the patient's symptoms resolve. Repeat testing shows a total bilirubin concentration of 1.5 mg/dL. Which of the following changes most likely contributed to this patient's hyperbilirubinemia?

	Hepatocyte bilirubin storage	Hepatocyte bilirubin excretion	Bilirubin conjugation	
<input type="radio"/> A.	Decreased	Decreased	Decreased	(13%)
<input type="radio"/> B.	Decreased	Increased	Increased	(5%)
<input type="radio"/> C.	Increased	Decreased	Normal	(11%)
<input type="radio"/> D.	Increased	Increased	Normal	(3%)
<input type="radio"/> E.	Increased	Normal	Decreased	(12%)
<input checked="" type="radio"/> F.	Normal	Normal	Decreased	(53%)







## Gilbert syndrome

<b>Epidemiology</b>	<ul style="list-style-type: none"><li>• Most common inherited disorder of bilirubin metabolism</li></ul>
<b>Pathogenesis</b>	<ul style="list-style-type: none"><li>• ↓ Hepatic UDP glucuronosyltransferase activity → ↓ conjugation of bilirubin</li></ul>
<b>Clinical findings</b>	<ul style="list-style-type: none"><li>• Recurrent episodes of mild jaundice</li><li>• Provoked by stress (eg, febrile illness, fasting, dehydration, vigorous exercise, menstruation, surgery)</li></ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"><li>• ↑ Unconjugated bilirubin (ie, indirect hyperbilirubinemia)</li><li>• Normal CBC, blood smear, reticulocyte count</li><li>• Normal AST, ALT, alkaline phosphatase</li></ul>
<b>Treatment</b>	<ul style="list-style-type: none"><li>• Benign; no treatment required</li></ul>

**ALT** = alanine aminotransferase; **AST** = aspartate aminotransferase; **CBC** = complete blood count; **UDP** = uridine diphosphogluconurate.

This patient had self-resolving scleral icterus and **isolated indirect hyperbilirubinemia** associated with a period of stress. These findings are consistent with **Gilbert syndrome**, the most common inherited disorder of bilirubin metabolism.





disorder of bilirubin metabolism.

**Normal bilirubin metabolism** begins with hepatic uptake of unconjugated bilirubin produced from red blood cell turnover. Within the liver, UDP glucuronosyltransferase conjugates bilirubin with glucuronic acid, after which conjugated bilirubin is excreted into bile canaliculi.

In **Gilbert syndrome**, a genetic mutation results in reduced enzymatic activity of UDP glucuronosyltransferase and therefore **decreased bilirubin conjugation (Choices B and D)**. Triggers associated with increased bilirubin production (eg, stress, illness, hemolysis) result in **episodic exacerbations** of indirect hyperbilirubinemia, as seen in this patient. Because **bilirubin excretion** into the bile duct is normal in Gilbert syndrome, **hepatocyte bilirubin storage** is also **normal**, as is liver histology **(Choices A and E)**.

Notably, impaired bilirubin conjugation also occurs in Crigler-Najjar syndrome, but patients typically have severe, chronic hyperbilirubinemia that begins in the neonatal period and can be associated with bilirubin-induced neurologic dysfunction.

**(Choice C)** Dubin-Johnson syndrome is a benign, inherited disorder of bilirubin metabolism characterized by defective hepatic excretion of bilirubin into the biliary system. Bilirubin conjugation is normal, but defective excretion results in increased hepatocyte storage of bilirubin, resulting in dense liver





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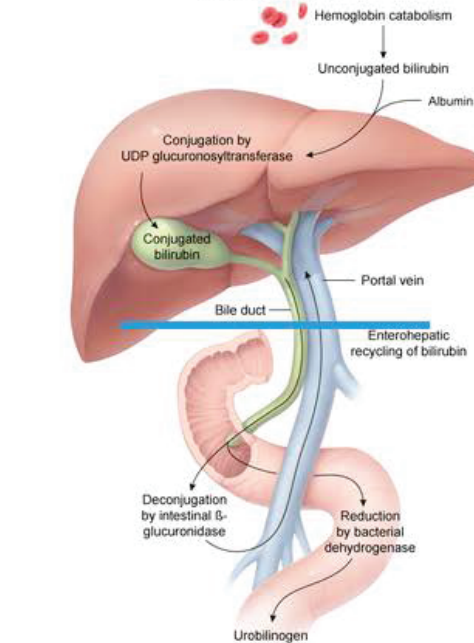
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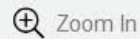
## Exhibit Display

## Bilirubin metabolism

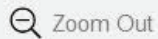


UDP = uridine diphosphoglucuronate.

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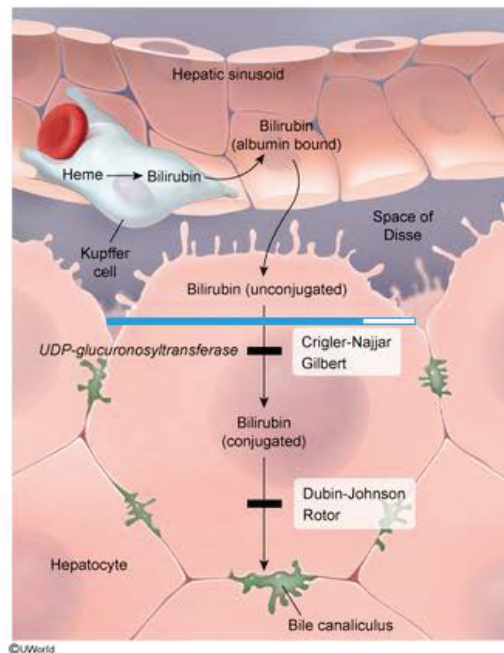
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## Exhibit Display

## Bilirubin metabolism



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**(Choices A and E).**

Notably, impaired bilirubin conjugation also occurs in Crigler-Najjar syndrome, but patients typically have severe, chronic hyperbilirubinemia that begins in the neonatal period and can be associated with bilirubin-induced neurologic dysfunction.

**(Choice C)** Dubin-Johnson syndrome is a benign, inherited disorder of bilirubin metabolism characterized by defective hepatic excretion of bilirubin into the biliary system. Bilirubin conjugation is normal, but defective excretion results in increased hepatocyte storage of bilirubin, resulting in dense liver pigmentation. Although patients often have recurrent episodes of scleral icterus, elevated direct bilirubin is expected due to reflux of conjugated bilirubin back into the plasma.

**Educational objective:**

Gilbert syndrome is characterized by indirect hyperbilirubinemia due to decreased bilirubin conjugation. Patients have recurrent, self-resolving episodes of scleral icterus and jaundice triggered by stress.

Pathophysiology

Subject

Gastrointestinal &amp; Nutrition

System

Hereditary hyperbilirubinemias

Topic

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A 41-year-old woman comes to the office due to a 6-month history of increasingly severe fatigue and malaise. For the past 5 years, she has lived on a small farm and eats only vegetables, fruits, and grains that she grows herself. Medical history is unremarkable. The patient takes no medications or nutritional supplements. She does not use tobacco or alcohol. This patient is at increased risk for deficiencies of which of the following nutrients?



- |                          | <b>Folic acid</b> | <b>Iron</b> | <b>Thiamine</b> | <b>Vitamin B<sub>12</sub></b> |
|--------------------------|-------------------|-------------|-----------------|-------------------------------|
| <input type="radio"/> A. | No                | No          | No              | Yes                           |
| <input type="radio"/> B. | No                | No          | Yes             | Yes                           |
| <input type="radio"/> C. | No                | Yes         | No              | Yes                           |
| <input type="radio"/> D. | Yes               | No          | Yes             | Yes                           |
| <input type="radio"/> E. | Yes               | Yes         | No              | No                            |
| <input type="radio"/> F. | Yes               | Yes         | Yes             | Yes                           |







malaise. For the past 5 years, she has lived on a small farm and eats only **vegetables**, **fruits**, and **grains** that she grows herself. Medical history is unremarkable. The patient takes no medications or nutritional supplements. She does not use tobacco or alcohol. This patient is at increased risk for deficiencies of which of the following nutrients?

	Folic acid	Iron	Thiamine	Vitamin B <sub>12</sub>	
 <input checked="" type="radio"/> A.	No	No	No	Yes	(24%)
<input type="radio"/> B.	No	No	Yes	Yes	(5%)
 <input type="radio"/> C.	No	Yes	No	Yes	(54%)
<input type="radio"/> D.	Yes	No	Yes	Yes	(4%)
<input type="radio"/> E.	Yes	Yes	No	No	(3%)
<input type="radio"/> F.	Yes	Yes	Yes	Yes	(7%)

**Incorrect**

Correct answer



54%

Answered correctly



02 mins, 10 secs

Time spent



03/04/2021

Last updated

Block Time Remaining: 00:04:42

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block



### Vegan diet

<b>Composition</b>	<ul style="list-style-type: none"><li>• Complete abstinence from animal-derived foods</li><li>• Emphasis on fruits, vegetables, legumes</li></ul>
<b>Potential benefits</b>	<ul style="list-style-type: none"><li>• Lower blood glucose &amp; cholesterol</li><li>• Reduced risk of cardiovascular disease (eg, heart disease, stroke)</li></ul>
<b>Potential nutritional deficiencies</b>	<ul style="list-style-type: none"><li>• Common: vitamin B<sub>12</sub>, vitamin D, calcium</li><li>• Possible: iodine, iron, zinc</li></ul>

A **vegan diet** is characterized by abstinence from **all animal-sourced products**. It differs from a simple vegetarian diet in that most vegetarians consume some nonmeat animal products (eg, milk, eggs). A vegan diet is typically plentiful in most vitamins (eg, A, B complex [except B<sub>12</sub>], C), minerals (eg, potassium, magnesium), and soluble fiber. Although most single plant-based protein sources (except soy) are deficient in certain essential amino acids, requirements can be met with a mixed (eg, legumes plus grains) vegan diet.





However, individuals on a vegan diet are at increased risk for the following:

- **Cobalamin (vitamin B<sub>12</sub>) deficiency:** It may take years to develop in those with large baseline B<sub>12</sub> stores; manifestations include megaloblastic anemia and subacute combined degeneration of the dorsal columns of the spinal cord.
- **Iron deficiency:** Many plant products (eg, leafy green vegetables) provide iron, but the quantity is often inadequate for those with increased iron requirements (eg, growing children, menstruating women) **(Choice A)**.
- **Calcium and vitamin D deficiency:** Most people obtain a significant amount of calcium and vitamin D from dairy and other animal-sourced products; individuals on a vegan diet often consume less of these nutrients than nonvegans, so supplementation may be necessary to prevent osteoporosis, especially in those without significant sunlight exposure (sunlight typically accounts for approximately 200-400 IU/day of a requirement of 600 IU/day).

This patient developed fatigue and malaise following years on a limited vegan diet. Although many commercially prepared vegan products are fortified with additional vitamins and minerals, this patient is consuming unprocessed foods only. She likely has anemia due to deficiency of iron and/or vitamin B<sub>12</sub>.







these nutrients than nonvegans, so supplementation may be necessary to prevent osteoporosis, especially in those without significant sunlight exposure (sunlight typically accounts for approximately 200-400 IU/day of a requirement of 600 IU/day).

This patient developed fatigue and malaise following years on a limited vegan diet. Although many commercially prepared vegan products are fortified with additional vitamins and minerals, this patient is consuming unprocessed foods only. She likely has anemia due to deficiency of iron and/or vitamin B<sub>12</sub>.

**(Choices B, D, E, and F)** Folic acid and thiamine (vitamin B<sub>1</sub>) are abundant in plant-based foods.

Deficiency may occur in individuals with abnormal dietary habits (eg, some individuals with alcohol abuse) but is uncommon in those consuming a variety of fruits, vegetables, and grains.

### Educational objective:

A vegan diet is characterized by abstinence from all animal-sourced products. Individuals on a vegan diet are commonly deficient in calcium, vitamin D, vitamin B<sub>12</sub>, and iron and may require supplementation.

Pathophysiology

Subject

Gastrointestinal & Nutrition

System

Vitamin b12 deficiency

Topic

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A 70-year old man comes to the office due to persistent aspiration. Two weeks ago, he had a stroke that impacted his speech, voice, and swallowing. Modified barium swallow study reveals aspiration of liquids without nasal regurgitation. Aspiration is ameliorated when the patient flexes his neck to put his chin to his chest during swallowing. This maneuver is most likely augmenting which of the following airway-protective mechanisms?

- ☐ A. Improvement of mastication
- ☐ B. Elevation of the soft palate
- ☐ C. Contraction of the base of tongue
- ☐ D. Superior displacement of the larynx
- ☐ E. Adduction of the vocal folds

Submit





A 70-year old man comes to the office due to persistent aspiration. Two weeks ago, he had a stroke that impacted his speech, voice, and swallowing. Modified barium swallow study reveals aspiration of liquids without nasal regurgitation. Aspiration is ameliorated when the patient flexes his neck to put his chin to his chest during swallowing. This maneuver is most likely augmenting which of the following airway-protective mechanisms?

- ☐ A. Improvement of mastication (0%)
- ☐ B. Elevation of the soft palate (0%)
- ☐ C. Contraction of the base of tongue (0%)
- ☒ D. Superior displacement of the larynx (100%)
- ☐ E. Adduction of the vocal folds (0%)

Correct

Collecting Statistics



01 min, 20 secs  
Time Spent



03/10/2021  
Last Updated







Normal **swallowing** involves a complex sequence of voluntary and reflexive processes that move food from the mouth to the esophagus while preventing it from entering the airway (ie, aspiration). Three main **airway-protective movements** occur during **normal swallowing**:

- **Displacement of the larynx superiorly** and anteriorly under the base of tongue, which allows food to be directed into the more posteriorly located esophagus
- **Tilting of the epiglottis** to block the airway
- Closing of the glottis by **adduction of the vocal folds**

Because of the complexity of swallowing, patients who sustain **strokes** often have persistent **dysphagia and/or aspiration**. If a neurologic deficit cannot be corrected, behavioral modifications can sometimes improve the safety of swallowing. A **chin-tuck maneuver** (ie, flexion of the head and neck during swallowing) sometimes helps. The maneuver seems to decrease the distance from the hyoid bone to the larynx (**simulating elevation of the larynx**), as well as to narrow the distance of the laryngeal entrance, leading to decreased aspiration.

**(Choice A)** The first phase of swallowing is the oral preparatory phase, in which food is chewed and mixed with saliva to form a controlled bolus. Although impaired mastication can lead to poor bolus formation





leading to decreased aspiration.

**(Choice A)** The first phase of swallowing is the oral preparatory phase, in which food is chewed and mixed with saliva to form a controlled bolus. Although impaired mastication can lead to poor bolus formation, flexion of the head and neck does not generally change the mechanics of mastication.

**(Choice B)** Elevation of the soft palate primarily prevents food from entering the nasopharynx rather than the larynx.

**(Choice C)** Contraction of the base of tongue occurs during the pharyngeal phase of swallowing and pushes the bolus posteriorly into the pharynx. Head and neck flexion could potentially worsen this function by increasing the distance that the base of tongue has to contract and by increasing the anterior force on the tongue due to gravity.

**(Choice E)** Although adduction of the vocal folds is an important airway-protective mechanism, head and neck flexion would not alter vocal fold movement.

### Educational objective:

The most important airway-protective movements during swallowing are the anterior/superior displacement of the larynx, the tilting of the epiglottis to block the airway, and vocal fold adduction. A chin-tuck maneuver can be helpful in some patients with aspiration by simulating the airway-protective movement of the larynx.





**(Choice B)** Elevation of the soft palate primarily prevents food from entering the nasopharynx rather than the larynx.

**(Choice C)** Contraction of the base of tongue occurs during the pharyngeal phase of swallowing and pushes the bolus posteriorly into the pharynx. Head and neck flexion could potentially worsen this function by increasing the distance that the base of tongue has to contract and by increasing the anterior force on the tongue due to gravity.

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The most important airway-protective movements during swallowing are the anterior/superior displacement of the larynx, the tilting of the epiglottis to block the airway, and vocal fold adduction. A chin-tuck maneuver can be helpful in some patients with aspiration by simulating the airway-protective movement of the larynx.

Physiology

Subject

Gastrointestinal &amp; Nutrition

System

Dysphagia

Topic

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An 87-year-old woman comes to the office to discuss treatment for colon cancer, which was recently diagnosed by colonoscopy. CT scan was negative for metastatic disease. The patient has no other medical conditions, and family history is unremarkable. She does not drink alcohol. Vital signs are normal. A chemotherapy regimen containing a medication that is primarily metabolized by the liver is chosen for therapy. Because of the patient's age, the physician is considering adjusting the dose to prevent adverse effects. Which of the following parameters is likely to be the most similar between this patient and a healthy 40-year-old individual?

- ☐ A. Hepatic concentration of cytochrome P-450
- ☐ B. Liver blood perfusion
- ☐ C. Rate of hepatic regeneration
- ☐ D. Serum aminotransferase levels
- ☐ E. Size of the liver

**Submit**



An 87-year-old woman comes to the office to discuss treatment for **colon cancer**, which was recently diagnosed by **colonoscopy**. CT scan was negative for metastatic disease. The patient has no other medical conditions, and family history is unremarkable. She does not drink alcohol. Vital signs are normal. A chemotherapy regimen containing a medication that is primarily metabolized by the liver is chosen for therapy. Because of the patient's age, the physician is considering adjusting the dose to prevent adverse effects. Which of the following parameters is likely to be the most similar between this patient and a healthy 40-year-old individual?

- ☐ A. Hepatic concentration of cytochrome P-450 (0%)
- ☐ B. Liver blood perfusion (0%)
- ☐ C. Rate of hepatic regeneration (0%)
- ☒ D. Serum aminotransferase levels (100%)
- ☐ E. Size of the liver (0%)

Incorrect





Effect of aging on the liver	
Anatomic changes	<ul style="list-style-type: none"><li>• Decreased liver size/mass<ul style="list-style-type: none"><li>◦ Due to decreased hepatic perfusion</li></ul></li></ul>
Physiologic changes	<ul style="list-style-type: none"><li>• Decreased regenerative capacity</li><li>• Decreased activity of cytochrome P-450 system</li><li>• Decreased protein (eg, albumin, clotting factors) synthesis</li></ul>
Histologic changes	<ul style="list-style-type: none"><li>• Increased hepatocyte size</li><li>• Increased polyploidy</li><li>• Accumulation of lipofuscin (brown atrophy)</li></ul>

A number of **age-related changes** take place in the liver that impair its ability to metabolize drugs. These changes place elderly individuals, such as this patient, at higher risk for drug-related toxicity. Normal age-related changes include the following:

- **Decreased liver mass**, which is largely explained by the **decrease in hepatic blood flow** that occurs with aging, can impair metabolism because the liver is unable to take up as much drug from the







related changes include the following.

- **Decreased liver mass**, which is largely explained by the **decrease in hepatic blood flow** that occurs with aging, can impair metabolism because the liver is unable to take up as much drug from the systemic circulation as it once could.
- **Decreased cytochrome P-450** expression and concentration slows the rate of hepatic metabolism of numerous drugs (eg, some antineoplastic agents).
- **Reduced rate of hepatic regeneration** impairs the liver's ability to recover after injury.

Although the liver's metabolic capabilities generally decline with age, **aminotransferase levels are unchanged** in healthy elderly individuals. Elevations in liver enzymes should therefore raise suspicion for undiagnosed hepatic disease or hepatotoxin exposure. Small variations may be seen in bilirubin, alkaline phosphatase, and gamma-glutamyltransferase levels, but they are generally minimal.

**(Choices A, B, C, and E)** Concentration of cytochrome P-450 and the liver's perfusion, regenerative capabilities, and size are all decreased in the elderly compared to younger individuals.

#### **Educational objective:**

A number of changes occur in the liver with aging that can affect drug metabolism. Typical changes include decreased liver mass and blood flow, decreased cytochrome P-450 expression and concentration, and





- **Reduced rate of hepatic regeneration** impairs the liver's ability to recover after injury.

Although the liver's metabolic capabilities generally decline with age, **aminotransferase levels are unchanged** in healthy elderly individuals. Elevations in liver enzymes should therefore raise suspicion for undiagnosed hepatic disease or hepatotoxin exposure. Small variations may be seen in bilirubin, alkaline phosphatase, and gamma-glutamyltransferase levels, but they are generally minimal.

**(Choices A, B, C, and E)** Concentration of cytochrome P-450 and the liver's perfusion, regenerative capabilities, and size are all decreased in the elderly compared to younger individuals.

### Educational objective:

A number of changes occur in the liver with aging that can affect drug metabolism. Typical changes include decreased liver mass and blood flow, decreased cytochrome P-450 expression and concentration, and reduced hepatic regeneration after injury. However, hepatic aminotransferase levels are unchanged.

### References

- [Liver physiology and liver diseases in the elderly.](#)

Physiology

Gastrointestinal &amp; Nutrition

Aging

Subject

System

Topic





A 4-day-old boy is brought to the office due to a 2-day history of progressive jaundice. The patient was born at term following an uncomplicated pregnancy. He is formula fed. The patient and his mother are both blood group A, Rh-positive. Vital signs are normal. Examination shows scleral icterus and jaundice over the face and chest. Laboratory results are as follows:

Hemoglobin 17.5 g/dL

Total bilirubin 8 mg/dL

Indirect bilirubin 7.2 mg/dL

The patient is followed closely, and the jaundice resolves without intervention in 3 days. This patient's jaundice was most likely the result of which of the following changes in bilirubin metabolism compared to an adult?

**Bilirubin production**   **Bilirubin conjugation**   **Enterohepatic bilirubin circulation**

☐ A. Decreased   ☐ B. Increased   ☐ C. Decreased







indirect bilirubin 7.2 mg/dL

The patient is followed closely, and the jaundice resolves without intervention in 3 days. This patient's jaundice was most likely the result of which of the following changes in bilirubin metabolism compared to an adult?

Bilirubin production	Bilirubin conjugation	Enterohepatic bilirubin circulation
-------------------------	--------------------------	---

- ☐ A. Decreased Increased Decreased
- ☐ B. Increased Decreased Decreased
- ☐ C. Increased Decreased Increased
- ☐ D. Increased Increased Increased
- ☐ E. Unchanged Increased Decreased

**Submit**



indirect bilirubin

7.2 mg/dL

The patient is followed closely, and the jaundice resolves without intervention in 3 days. This patient's jaundice was most likely the result of which of the following changes in bilirubin metabolism compared to an adult?

Bilirubin production	Bilirubin conjugation	Enterohepatic bilirubin circulation
----------------------	-----------------------	-------------------------------------

- ☐ A. Decreased Increased Decreased (0%)
- ☒ B. Increased Decreased Decreased (0%)
- ☐ C. Increased Decreased Increased (100%)
- ☐ D. Increased Increased Increased (0%)
- ☐ E. Unchanged Increased Decreased (0%)

Incorrect

02 mins, 25 secs

03/12/2021

Block Time Remaining: 00:02:26

TUTOR

<https://t.me/USMLEWorldStep1>

0



Feedback



Suspend

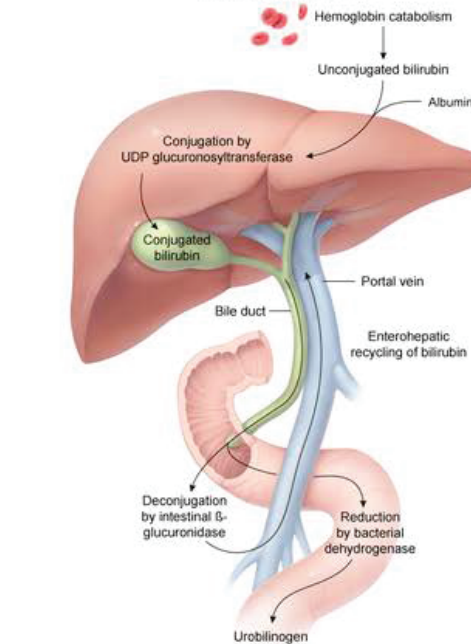


End Block



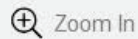
## Exhibit Display

## Bilirubin metabolism

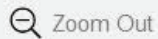


UDP = uridine diphosphoglucuronate.

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Zoom In



Zoom Out



Reset



New | Existing



My Notebook







UDP = uridine diphosphogluconate.

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This newborn had **elevated indirect bilirubin** levels with jaundice that **self-resolved** in the first week of life, findings consistent with **benign neonatal hyperbilirubinemia**.

Normally, unconjugated bilirubin is released into the bloodstream upon breakdown of red blood cells (RBCs) and taken up by the liver. Hepatic UDP glucuronosyltransferase then conjugates bilirubin, which is secreted into bile and excreted into the intestines. Bacterial enzymes in the intestines then reduce bilirubin to urobilinogen, allowing for excretion through the urine and stool.

Benign neonatal hyperbilirubinemia is caused by several **physiologic differences** in bilirubin metabolism **in newborns** as compared to those in older children and adults.

- First, **bilirubin production is increased** due to increased breakdown of fetal RBCs, which are high in number (hematocrit up to 60%) and have a shorter life span (90 days as compared to 120 days in adults).
- Second, **bilirubin conjugation is decreased** due to physiologically lower levels of UDP glucuronosyltransferase in the immature neonatal liver.
- Finally, relative gut sterility in newborns results in decreased reduction of bilirubin to urobilinogen; instead, intestinal  $\beta$ -glucuronidase (which is synthesized both endogenously and by gut bacteria)





adults).

- Second, **bilirubin conjugation is decreased** due to physiologically lower levels of UDP glucuronosyltransferase in the immature neonatal liver.
- Finally, relative gut sterility in newborns results in decreased reduction of bilirubin to urobilinogen; instead, intestinal  $\beta$ -glucuronidase (which is synthesized both endogenously and by gut bacteria) deconjugates the bilirubin which allows it to be reabsorbed, therefore **increasing enterohepatic circulation**.

### Educational objective:

Pathophysiology of benign neonatal hyperbilirubinemia involves increased bilirubin production and decreased bilirubin conjugation as well as increased enterohepatic circulation. Indirect hyperbilirubinemia and jaundice typically peak in the first few days of life and usually resolve without intervention.

### References

- [Neonatal jaundice.](#)
- [Neonatal jaundice.](#)

Biochemistry

Gastrointestinal & Nutrition

Neonatal jaundice

Block Time Remaining: 00:02:26

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block



A 6-year-old boy is brought to the emergency department due to abrupt-onset vomiting, lethargy, and altered mental status. For 4 days, the patient has had a fever, cough, and rhinorrhea, which were treated symptomatically with aspirin. He has no prior medical conditions, and his family history is unremarkable. Vital signs are normal. The patient is stuporous and does not respond to verbal commands. Hepatomegaly is present. There is no jaundice. Laboratory results are as follows:

#### Liver function studies

Total bilirubin 1.2 mg/dL

Alkaline phosphatase 150 U/L

Aspartate aminotransferase (SGOT) 2,431 U/L

Alanine aminotransferase (SGPT) 3,402 U/L

#### Coagulation studies

PT 30 sec

Activated PTT 68 sec







PT

30 sec

Activated PTT

68 sec

Blood, plasma, and serum

Ammonia

462  $\mu\text{g/dL}$ 

Which of the following is the most likely cause of this patient's presentation?

- ☐ A. Accumulation of a misfolded protein within hepatocytes
- ☐ B. CD8<sup>+</sup> T-cell-mediated destruction of viral infected hepatocytes
- ☐ C. Depletion of intracellular reduced glutathione
- ☐ D. Excessive formation of superoxide in hepatocytes
- ☐ E. Mitochondrial damage leading to impaired fatty acid metabolism

**Submit**



PT

30 sec

Activated PTT

68 sec

Blood, plasma, and serum

Ammonia

462  $\mu\text{g/dL}$ 

Which of the following is the most likely cause of this patient's presentation?

- ☐ A. Accumulation of a misfolded protein within hepatocytes (0%)
- ☐ B. CD8<sup>+</sup> T-cell-mediated destruction of viral infected hepatocytes (0%)
- ☐ C. Depletion of intracellular reduced glutathione (0%)
- ☐ D. Excessive formation of superoxide in hepatocytes (0%)
- ☒ E. Mitochondrial damage leading to impaired fatty acid metabolism (100%)

Correct

Collecting Statistics



01 min, 28 secs

Time Spent



03/24/2021

Last Updated

Block Time Remaining: 00:01:28

TUTOR

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block



Reye syndrome	
<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>• Aspirin use in children during viral infection (eg, influenza, varicella)</li> <li>• Mitochondrial toxicity → impaired fatty acid metabolism</li> <li>• Microvesicular fat deposits in the liver</li> <li>• Hepatic dysfunction → hyperammonemia</li> <li>• Diffuse astrocyte swelling (ie, cerebral edema)</li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>• Acute liver failure               <ul style="list-style-type: none"> <li>◦ Hepatomegaly</li> <li>◦ Elevated transaminases; coagulopathy</li> </ul> </li> <li>• Rapidly progressive encephalopathy               <ul style="list-style-type: none"> <li>◦ Vomiting, lethargy, seizures, coma</li> </ul> </li> </ul>
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Supportive</li> </ul>

This patient likely has **Reye syndrome**, a rapidly progressive disorder characterized by acute liver failure (eg, hepatomegaly, elevated transaminases, coagulopathy) and encephalopathy.

Reye syndrome most commonly occurs in children who are given salicylates (eg, aspirin) during a viral







Reye syndrome most commonly occurs in children who are given **salicylates** (eg, aspirin) during a **viral infection** (eg, influenza). In susceptible patients, salicylates can **damage mitochondria** within hepatocytes and inhibit enzymes involved in **fatty acid beta-oxidation**, the primary metabolic pathway hepatocytes depend on to maintain normal cellular function. Salicylate-induced hepatic injury prevents the liver from keeping up with metabolic demands, which often increase in the setting of a viral infection and predisposes patients to the development of **acute liver failure**.

Patients with Reye syndrome typically have vomiting and **encephalopathy** (eg, lethargy, altered mental status) related to the buildup of ammonia from liver failure. Seizures and coma may also occur. In addition to **hyperammonemia**, laboratory analysis typically shows markedly **elevated aminotransferases**, as seen in this patient. In addition, **PT** and **PTT** are often **prolonged** due to impaired hepatic synthetic function, but bilirubin is generally normal to slightly elevated. There is no specific treatment for Reye syndrome other than supportive care.

**(Choice A)** Alpha-1 antitrypsin (A1A) deficiency causes abnormal A1A protein folding and accumulation within hepatocytes. Although it can cause chronic liver disease in childhood, this patient's acute hepatic dysfunction and encephalopathy after salicylate exposure is more characteristic of Reye syndrome.

**(Choice B)** Viral hepatitis induces a robust CD8<sup>+</sup> T-cell response against infected hepatocytes, which





**(Choice B)** Viral hepatitis induces a robust CD8<sup>+</sup> T-cell response against infected hepatocytes, which typically leads to elevations in aminotransferases. Although viral hepatitis may cause acute liver failure, it would not be triggered by salicylate exposure. This patient also lacks typical risk factors for contracting hepatitis A (eg, fecal-oral transmission) or hepatitis B and C (eg, blood-borne pathogens).

**(Choice C)** Acetaminophen overdose can cause acute liver failure through the depletion of intracellular glutathione, leading to an overabundance of hepatotoxic metabolites (eg, N-acetyl-p-benzoquinone imine). Salicylates do not deplete intracellular glutathione like acetaminophen does.

**(Choice D)** Reperfusion after ischemic insult to the liver can create hepatotoxic reactive oxygen species, such as superoxide. Reperfusion injury occurs in the setting of profound hypotension (eg, septic shock), which is not present in this patient.

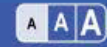
### Educational objective:

Reye syndrome is characterized by acute liver failure (eg, hepatomegaly, elevated aminotransferases, coagulopathy) and rapidly progressive encephalopathy related to hyperammonemia. It usually develops in susceptible children during a viral infection after administration of salicylates (eg, aspirin), which cause damage to the mitochondria and impair fatty acid beta-oxidation within hepatocytes.

### References







A 16-year-old girl is brought to the emergency department because of progressively increasing nausea, vomiting and right upper quadrant pain. She was initially seen in the emergency department 24 hours ago for nausea and vomiting but was discharged when her examination and laboratory studies were unremarkable. At today's visit, the patient reveals, "I am so upset. My boyfriend broke up with me and I have been taking a lot of pain medication to relieve my pain." Temperature is 37.1 C (98.8 F), blood pressure is 108/70 mm Hg, pulse is 102/min, and respirations are 16/min. Pulse oximetry is 98% on room air. On examination, scleral icterus and marked right upper quadrant tenderness are present. Pupils are normal in size and reactive to light. Neurologic examination shows no abnormalities. Laboratory results are as follows:

Total bilirubin	1.3 mg/dL
Alkaline phosphatase	120 U/L
Aspartate aminotransferase (SGOT)	3,906 U/L
Alanine aminotransferase (SGPT)	4,014 U/L

Which of the following is the most likely underlying mechanism of drug toxicity in this patient?







Total bilirubin	1.3 mg/dL
Alkaline phosphatase	120 U/L
Aspartate aminotransferase (SGOT)	3,906 U/L
Alanine aminotransferase (SGPT)	4,014 U/L

Which of the following is the most likely underlying mechanism of drug toxicity in this patient?

- ☐ A. Cytotoxic T-cell response to hepatocyte proteins
- ☐ B. Drug-mediated inhibition of bile flow
- ☐ C. Drug metabolite–induced mitochondrial dysfunction
- ☐ D. Drug–induced disruption of fatty acid metabolism
- ☐ E. Reactive oxygen species–induced stellate cell activation

Submit





Total bilirubin	1.3 mg/dL
Alkaline phosphatase	120 U/L
Aspartate aminotransferase (SGOT)	3,906 U/L
Alanine aminotransferase (SGPT)	4,014 U/L

Which of the following is the most likely underlying mechanism of drug toxicity in this patient?

- ☐ A. Cytotoxic T-cell response to hepatocyte proteins (0%)
- ☐ B. Drug-mediated inhibition of bile flow (0%)
- ☒ C. Drug metabolite-induced mitochondrial dysfunction (100%)
- ☐ D. Drug-induced disruption of fatty acid metabolism (0%)
- ☐ E. Reactive oxygen species-induced stellate cell activation (0%)

Incorrect

Correct answer

Collecting Statistics



01 min, 08 secs

Time spent



03/31/2021

Last updated

Block Time Remaining: 00:01:08

TUTOR

<https://t.me/USMLEWorldStep1>



0



Feedback



Suspend



End Block

**Acetaminophen overdose**

<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>• Depletion of intrahepatic glutathione → overaccumulation of NAPQI</li> <li>• NAPQI forms adduct with mitochondrial proteins → oxidative hepatocellular injury</li> </ul>
<b>Clinical features</b>	<ul style="list-style-type: none"> <li>• Initially asymptomatic or nonspecific (eg, nausea, vomiting, malaise)</li> <li>• Can progress to right upper quadrant pain, jaundice, hepatic encephalopathy &amp; bleeding diathesis</li> </ul>
<b>Laboratory findings</b>	<ul style="list-style-type: none"> <li>• Normal until 24 hr after ingestion</li> <li>• ↑↑ AST, ALT (often &gt;1,000 U/L)</li> <li>• ↑ PT, PTT when severe</li> <li>• ± Elevated bilirubin &amp; alkaline phosphatase</li> <li>• Liver biopsy: centrilobular necrosis</li> </ul>
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• N-acetylcysteine: repletes intrahepatic glutathione stores</li> </ul>







	<ul style="list-style-type: none"> <li>• <del>Elevated bilirubin &amp; alkaline phosphatase</del></li> <li>• Liver biopsy: centrilobular necrosis</li> </ul>
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• N-acetylcysteine: repletes intrahepatic glutathione stores</li> </ul>

**ALT** = alanine aminotransferase; **AST** = aspartate aminotransferase; **NAPQI** = N-acetyl-p-benzoquinone imine.

This patient who took large quantities of a pain medication initially had nausea and vomiting and has now developed scleral icterus, right upper quadrant pain, and markedly elevated aminotransferases. These findings are consistent with an overdose of **acetaminophen**, a commonly used analgesic.

When taken at appropriate doses, acetaminophen produces small amounts of the **toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI)**, which is conjugated with glutathione in the liver and excreted. At supratherapeutic doses, glutathione becomes saturated, allowing excessive amounts of NAPQI to form adducts with hepatic proteins that **disrupt hepatocyte mitochondrial function** and cause **oxidative injury**.

Because acetaminophen-induced liver injury primarily affects hepatocytes (ie, **hepatocellular liver injury**), laboratory findings show markedly **elevated aminotransferases** with levels sometimes >1,000 U/L. Mild elevations of bilirubin and alkaline phosphatase can be seen but may be normal. Liver biopsy shows

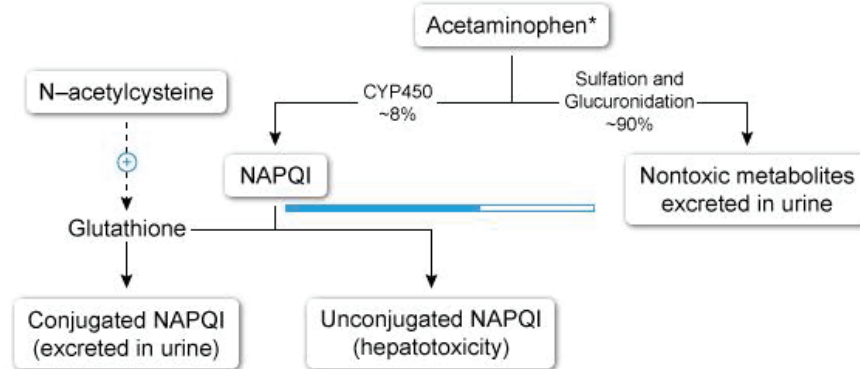




Elevated bilirubin & alkaline phosphatase

### Exhibit Display

## Hepatic metabolism of acetaminophen



\*2% of Acetaminophen is excreted unchanged in the urine.

CYP450 = Cytochrome p450.

NAPQI = N-acetyl-p-benzoquinoneimine.

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Zoom In



Zoom Out



Reset



New



Existing



My Notebook





Because acetaminophen-induced liver injury primarily affects hepatocytes (ie, **hepatocellular liver injury**), laboratory findings show markedly **elevated aminotransferases** with levels sometimes >1,000 U/L. Mild elevations of bilirubin and alkaline phosphatase can be seen but may be normal. Liver biopsy shows centrilobular hepatic necrosis, a common finding in ischemic or toxic liver injury.

**(Choice A)** Certain drugs (eg, carbamazepine, phenytoin) can trigger a robust CD4<sup>+</sup> and CD8<sup>+</sup> T-cell response against hepatic proteins, leading to drug reaction with eosinophilia and systemic symptoms (DRESS). Although hepatocellular liver injury can occur, fever, lymphadenopathy, and skin manifestations (eg, facial edema, coalescing erythema) would be expected.

**(Choice B)** Drug-mediated (eg, ceftriaxone) cholestatic liver injury typically causes biliary duct damage or interrupts the flow of bile. These patients have markedly elevated levels of alkaline phosphatase (and sometimes bilirubin), and aminotransferase levels are typically normal.

**(Choice D)** Microvesicular steatohepatitis, or small droplets of intracytoplasmic lipids within hepatocytes, is caused by drugs that disrupt fatty acid beta-oxidation. Ibuprofen and aspirin are commonly used analgesics that can rarely lead to this condition; however, marked aminotransferase elevations are not seen in ibuprofen toxicity, and aspirin toxicity is usually seen in young children with a recent viral infection (ie, Reye syndrome).







**(Choice D)** Microvesicular steatohepatitis, or small droplets of intracytoplasmic lipids within hepatocytes, is caused by drugs that disrupt fatty acid beta-oxidation. Ibuprofen and aspirin are commonly used analgesics that can rarely lead to this condition; however, marked aminotransferase elevations are not seen in ibuprofen toxicity, and aspirin toxicity is usually seen in young children with a recent viral infection (ie, Reye syndrome).

**(Choice E)** Chronic alcohol consumption can generate reactive oxygen species (ROS), which activate stellate cells and cause cirrhosis. Although NAPQI does create ROS, stellate cell activation does not occur, and this patient's acute liver injury after analgesic ingestion makes this diagnosis unlikely.

### Educational objective:

Excessive acetaminophen use causes toxicity through its metabolite N-acetyl-p-benzoquinone imine, which disrupts hepatocyte mitochondrial function and induces oxidative injury throughout the liver. The resulting hepatocellular liver injury markedly elevates aminotransferase, with levels sometimes exceeding 1,000 U/L.

Pharmacology

Subject

Pharmacology (General Principles)

System

Acetaminophen poisoning

Topic

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An 80-year-old man comes to the office for evaluation of persistent dry mouth and difficulty chewing food. He has had no dry eyes or joint pains. The patient has no chronic medical conditions and takes no medications. On examination, there is decreased saliva production but no tenderness or swelling of the salivary glands. Extensive dental caries are present. Laboratory results show negative anti-Ro/SSA and anti-La/SSB antibodies. Which of the following age-related changes is most likely responsible for this patient's symptoms?

- ☐ A. Acinar atrophy and fatty infiltration of salivary glands
- ☐ B. Acinar atrophy due to extracellular amyloid deposition
- ☐ C. Focal lymphocytic infiltration of the salivary glands
- ☐ D. Granulomatous inflammation of the salivary glands
- ☐ E. Neutrophilic inflammation of the salivary glands

**Submit**



An 80-year-old man comes to the office for evaluation of persistent dry mouth and difficulty chewing food. He has had no dry eyes or joint pains. The patient has no chronic medical conditions and takes no medications. On examination, there is decreased saliva production but no tenderness or swelling of the salivary glands. Extensive dental caries are present. Laboratory results show negative anti-Ro/SSA and anti-La/SSB antibodies. Which of the following age-related changes is most likely responsible for this patient's symptoms?

- ☒ A. Acinar atrophy and fatty infiltration of salivary glands (100%)
- ☐ B. Acinar atrophy due to extracellular amyloid deposition (0%)
- ☐ C. Focal lymphocytic infiltration of the salivary glands (0%)
- ☐ D. Granulomatous inflammation of the salivary glands (0%)
- ☐ E. Neutrophilic inflammation of the salivary glands (0%)

Correct

Collecting Statistics



01 min, 04 secs

Time Spent



04/01/2021

Last Updated

Block Time Remaining: 00:01:04

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block





### Age-related changes to the upper aerodigestive tract

<b>Salivary glands</b>	<ul style="list-style-type: none"> <li>• Acinar atrophy, fatty infiltration</li> <li>• Reduced saliva production</li> <li>• Xerostomia, dental caries</li> </ul>
<b>Oral/oropharyngeal muscles</b>	<ul style="list-style-type: none"> <li>• Decreased muscle mass &amp; tissue elasticity</li> <li>• Weakness &amp; dyscoordination of masticatory, tongue &amp; pharyngeal muscles</li> <li>• Increased transit time, decreased coordination</li> </ul>
<b>Other effects</b>	<ul style="list-style-type: none"> <li>• Mucosal atrophy</li> <li>• Decreased taste &amp; smell</li> <li>• Impaired airway protective reflexes</li> </ul>

Elderly patients are at increased risk of dysphagia due to age-related physiologic changes in the upper aerodigestive tract. **Acinar atrophy and fatty infiltration** affecting the parotid **salivary glands** result in a dramatic reduction (~50%) in saliva production, which frequently leads to xerostomia. This **decrease in saliva** is often accompanied by age-related mucosal atrophy, which manifests as receding gums with





aerodigestive tract. **Acinar atrophy and fatty infiltration** affecting the parotid **salivary glands** result in a

dramatic reduction (~50%) in saliva production, which frequently leads to xerostomia. This **decrease in saliva** is often accompanied by age-related mucosal atrophy, which manifests as receding gums with increased exposure of tooth roots; these changes increase the risk of **tooth decay** in elderly patients.

Elderly patients also commonly have a **decrease in muscle mass** and **loss of connective tissue elasticity**, which can impact the muscles of mastication, intrinsic and extrinsic tongue muscles, and pharyngeal constrictors. These alterations can lead to difficulty forming food into a bolus and propelling food from the oral cavity into the oropharynx and then into the esophagus.

In addition, elderly patients have a **decreased sense of taste and smell** and impaired **airway protective reflexes**. They also are more likely to have comorbid neurologic diseases (eg, stroke, Parkinson disease) that further increase the risk of dysphagia. Dysphagia can lead to **malnutrition** and **aspiration**, both of which cause significant morbidity and mortality in the elderly.

**(Choice B)** Involvement of the salivary glands by systemic amyloidosis is common, but amyloid deposition significant enough to lead to dysphagia is very rare; normal age-related physiologic changes are much more likely in this patient.

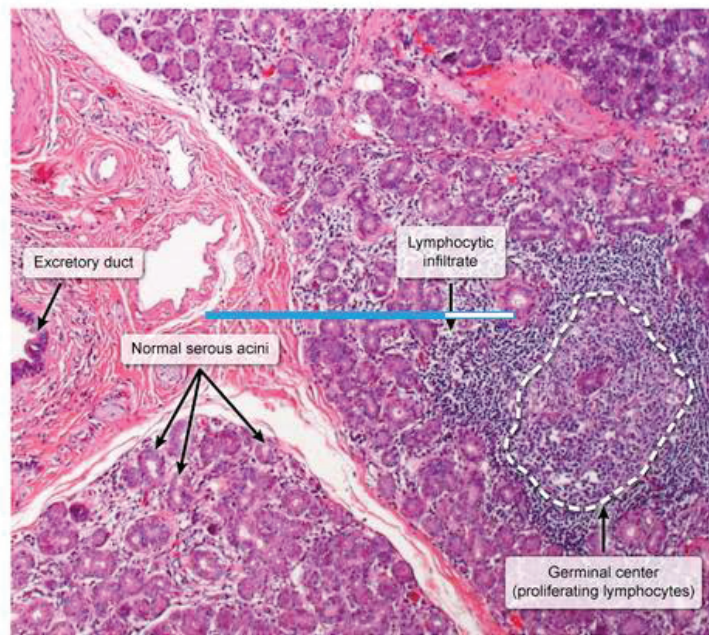
**(Choice C)** Fibrosis and focal **lymphocytic infiltration** into the salivary glands are seen in Sjögren



aerodigestive tract. Acinar atrophy and fatty infiltration affecting the parotid salivary glands result in a

## Exhibit Display

## Sjogren syndrome



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Zoom In



Zoom Out



Reset



New



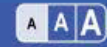
Existing



My Notebook







**(Choice C)** Fibrosis and focal **lymphocytic infiltration** into the salivary glands are seen in Sjögren syndrome, an autoimmune disease impacting **exocrine glands** (eg, salivary, lacrimal, vaginal). Although patients often have dry mouth, they also typically have dry eyes and positive anti-Ro/SSA and/or anti-La/SSB antibodies.

**(Choice D)** Granulomatous inflammation of the salivary glands is seen in uveoparotid fever (ie, Heerfordt syndrome), an uncommon manifestation of sarcoidosis characterized by acute fever, parotitis, and anterior uveitis.

**(Choice E)** Elderly patients with xerostomia are at risk of acute sialadenitis, an infection of the salivary glands caused by retrograde seeding of bacteria from the oral cavity. Patients have acute, typically unilateral salivary gland swelling, exquisite pain, and fever.

### Educational objective:

Elderly patients have decreased saliva production due to acinar atrophy and fatty infiltration of the salivary glands. Other age-related changes include oral mucosal atrophy; weakening of the muscles of mastication, tongue muscles, and pharyngeal constrictors; and a decreased sense of taste and smell. As a result, elderly patients are at increased risk of dysphagia, malnutrition, and pneumonia.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



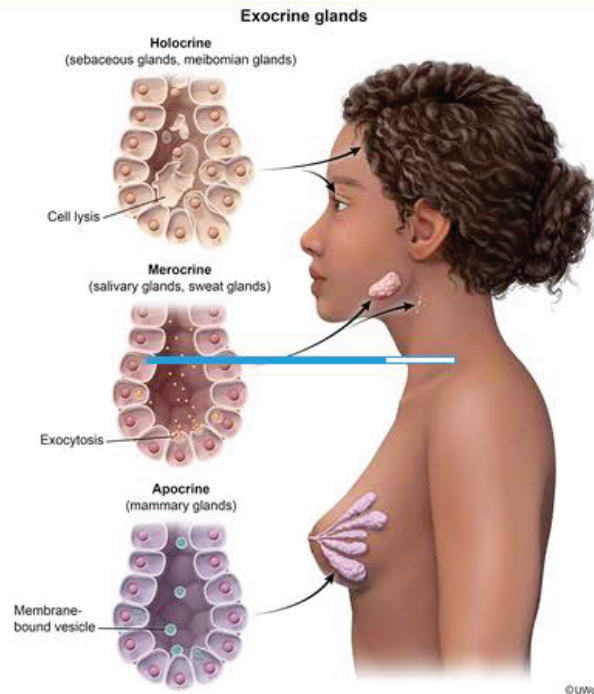
Text Zoom



Settings

(Choice C) Fibrosis and focal lymphocytic infiltration into the salivary glands are seen in Sjögren

### Exhibit Display



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Zoom In



Zoom Out



Reset



New | Existing



My Notebook



0



Feedback



Suspend



End Block